

(12) **United States Patent**
Wilson, Jr. et al.

(10) **Patent No.:** **US 12,281,148 B2**
(45) **Date of Patent:** ***Apr. 22, 2025**

(54) **ANTI-PD-1 ANTIBODY-ATTENUATED IL-2 IMMUNOCONJUGATES AND USES THEREOF**

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(73) Assignee: **Cephalon LLC**

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

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(65) **Prior Publication Data**

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Related U.S. Application Data

(63) Continuation of application No. 18/335,650, filed on Jun. 15, 2023.

(Continued)

(51) **Int. Cl.**
C07K 14/55 (2006.01)
C07K 16/28 (2006.01)

(52) **U.S. Cl.**
CPC **C07K 14/55** (2013.01); **C07K 16/2818** (2013.01); **C07K 2317/21** (2013.01);
(Continued)

(58) **Field of Classification Search**
CPC C07K 14/55; C07K 16/2818; C07K 2317/21; C07K 2317/75; C07K 2317/92; C07K 2319/33; C07K 2319/75
See application file for complete search history.

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Assistant Examiner — Laura Ann Essex

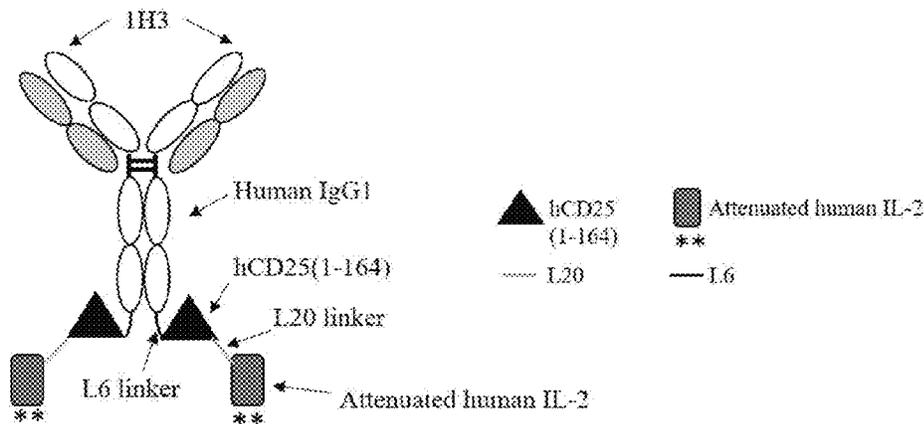
(74) *Attorney, Agent, or Firm* — BakerHostetler

(57) **ABSTRACT**

Disclosed herein are modified human interleukin-2 (hIL-2) proteins, human antibody molecules, or antigen-binding fragments thereof, that immunospecifically bind to human programmed cell death protein-1 (hPD-1), and immunoconjugates comprising the same.

10 Claims, 26 Drawing Sheets

Specification includes a Sequence Listing.



1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2

Related U.S. Application Data

(60) Provisional application No. 63/502,746, filed on May 17, 2023, provisional application No. 63/481,630, filed on Jan. 26, 2023, provisional application No. 63/352,842, filed on Jun. 16, 2022.

(52) **U.S. Cl.**
 CPC *C07K 2317/75* (2013.01); *C07K 2317/92* (2013.01); *C07K 2319/33* (2013.01); *C07K 2319/75* (2013.01)

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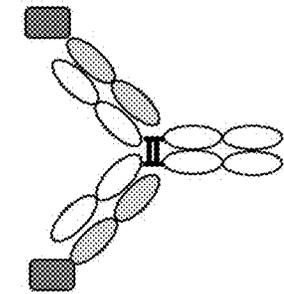
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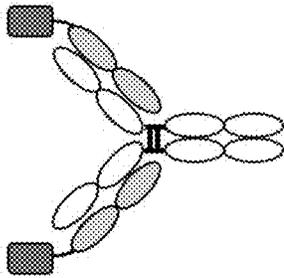
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FIG. 1A



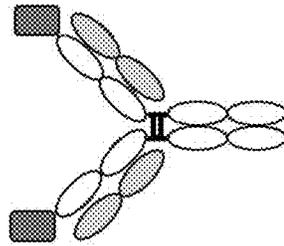
hIL-2 Nterm light chain df

FIG. 1B



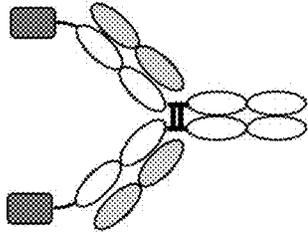
hIL-2 Nterm light chain L6 fusion

FIG. 1C



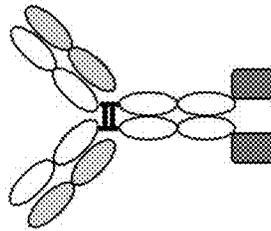
hIL-2 Nterm heavy chain df

FIG. 1D



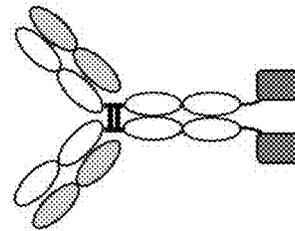
hIL-2 Nterm heavy chain L6 fusion

FIG. 1E



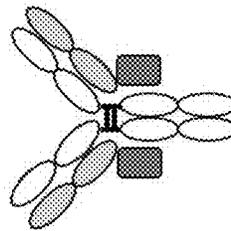
hIL-2 Cterm heavy chain df

FIG. 1F



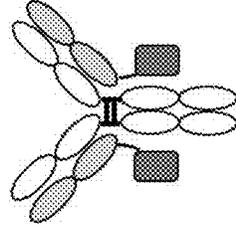
hIL-2 Cterm heavy chain L6 fusion

FIG. 1G



hIL-2 Cterm light chain df

FIG. 1H



hIL-2 Cterm light chain L6 fusion

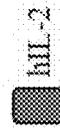


FIG. 2A

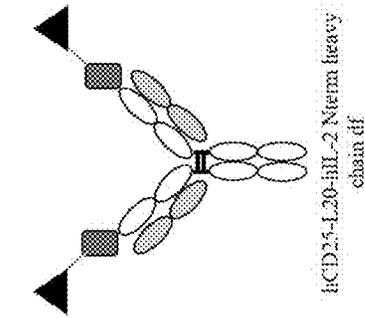


FIG. 2B

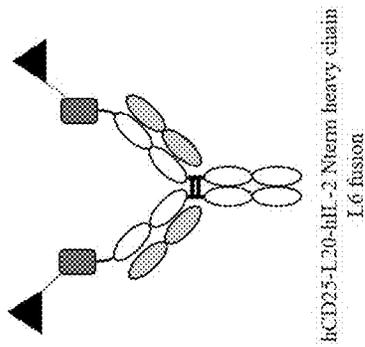


FIG. 2C

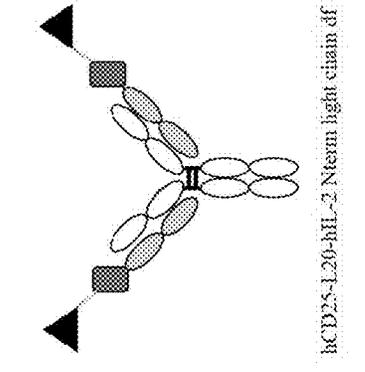


FIG. 2D

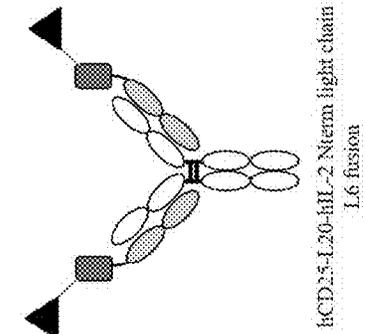


FIG. 2E

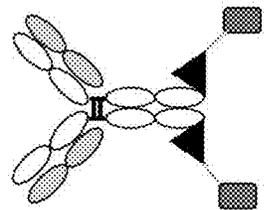


FIG. 2F

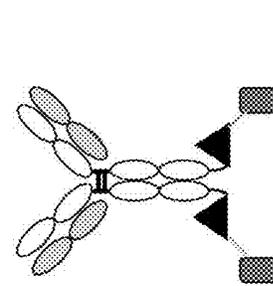


FIG. 2G

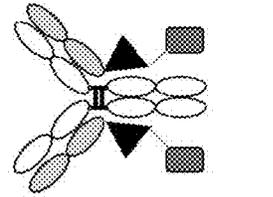


FIG. 2H

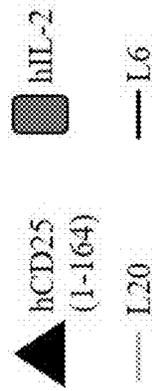
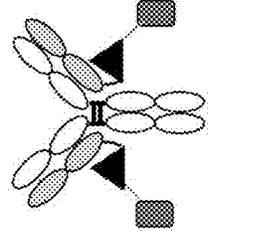
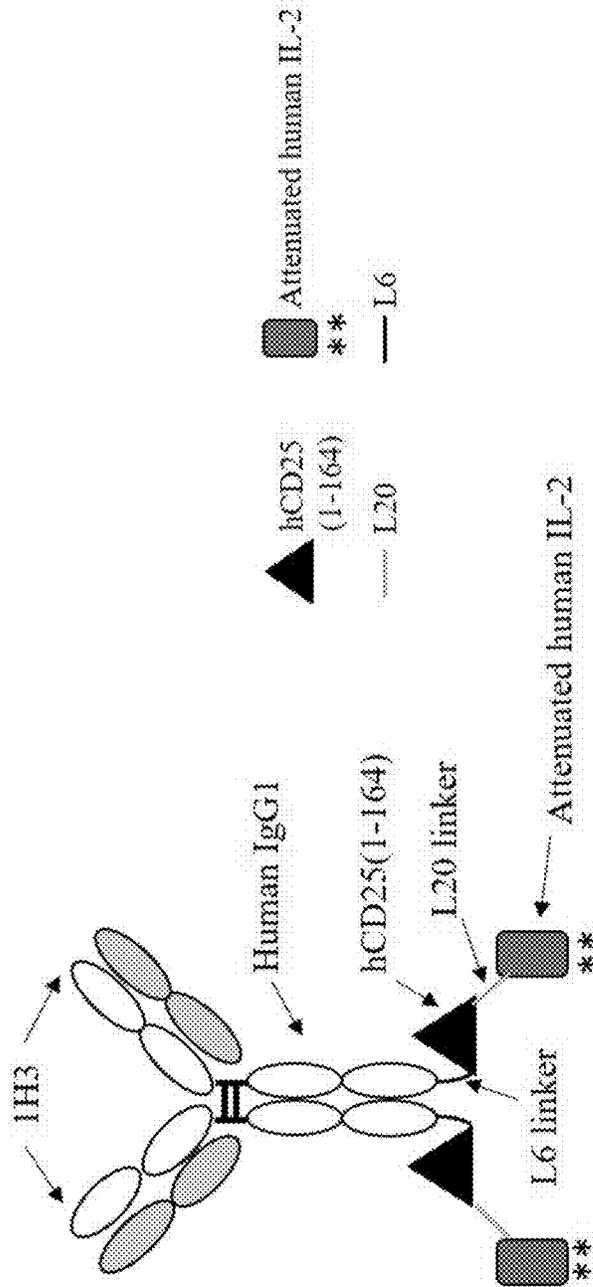


FIG. 3



IH3-hIgG1-L6-hCD25(1-164)-L20-hIL-2

FIG. 4B

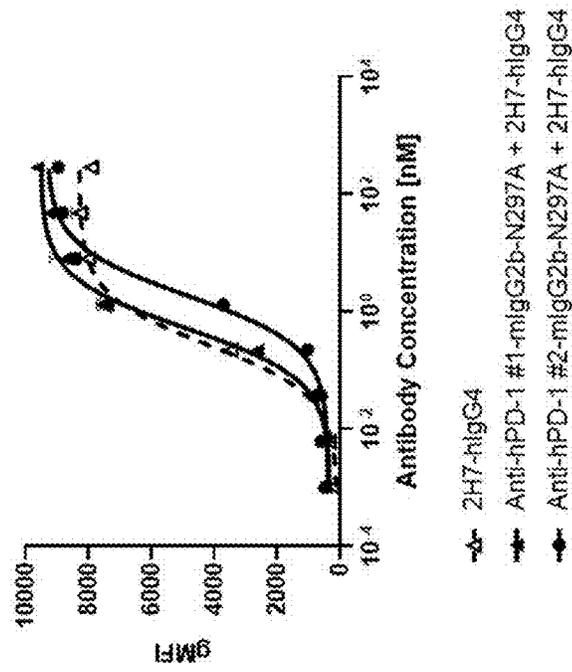


FIG. 4A

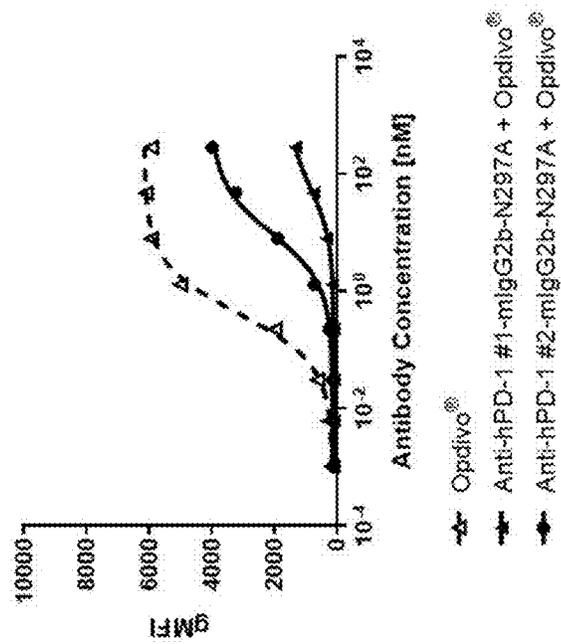


FIG. 4D

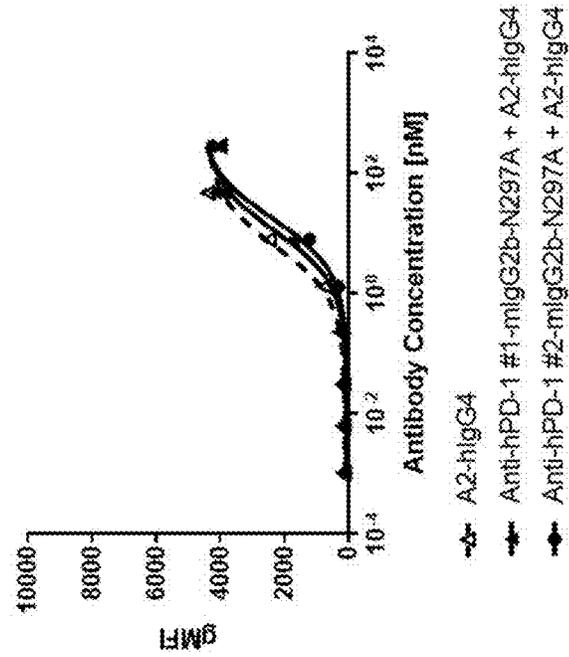


FIG. 4C

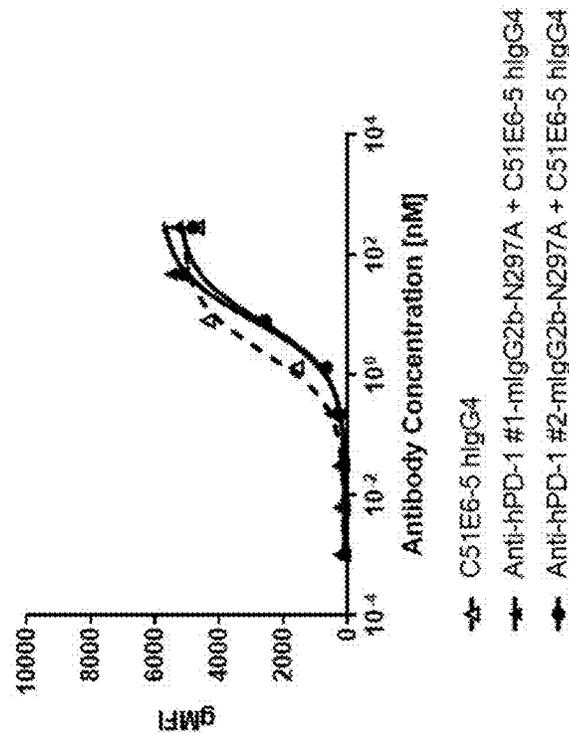


FIG. 5

Anti-hPD-1 antibody-attenuated hIL-2 fusions

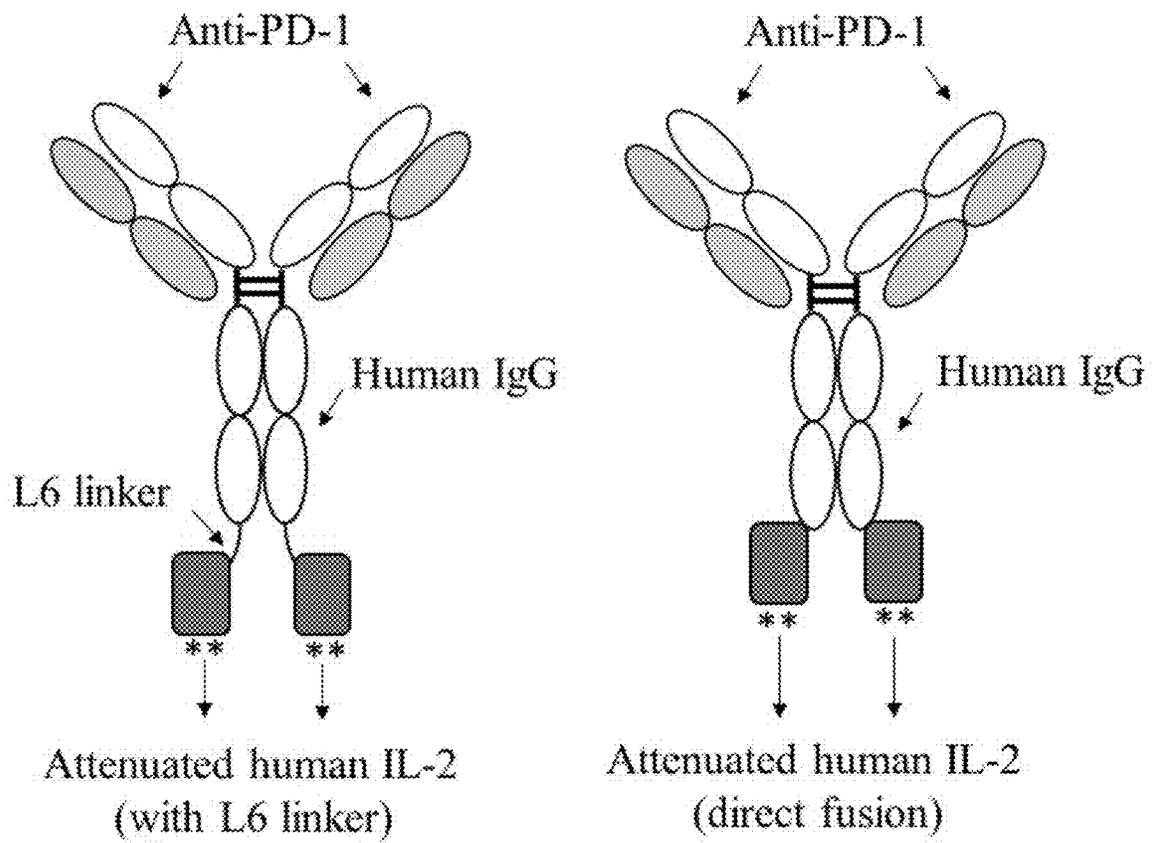
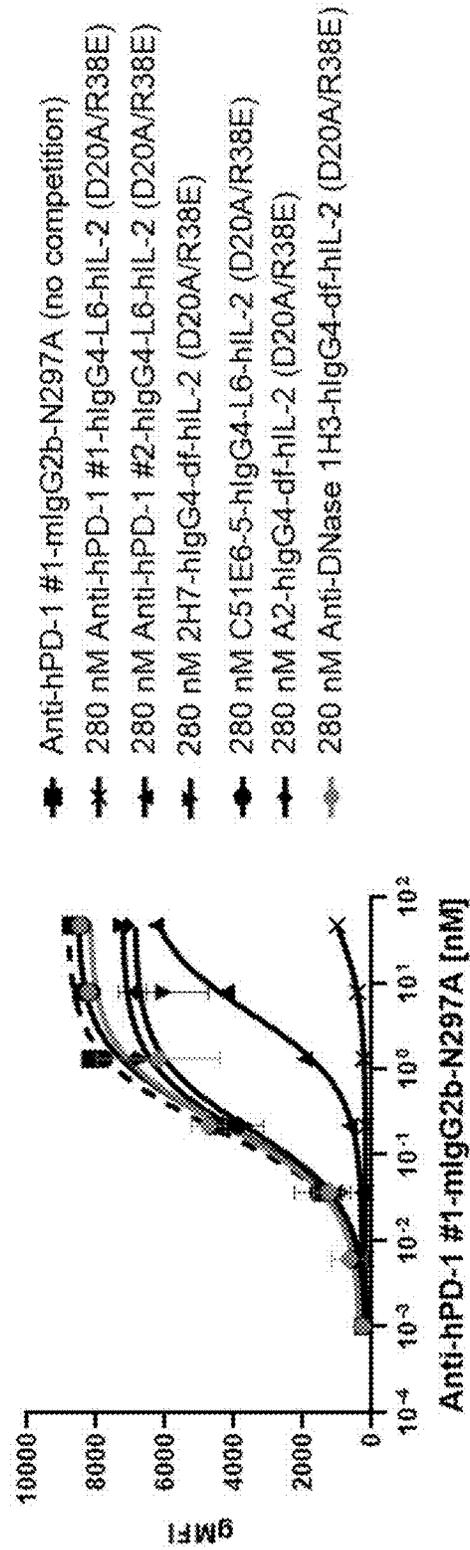
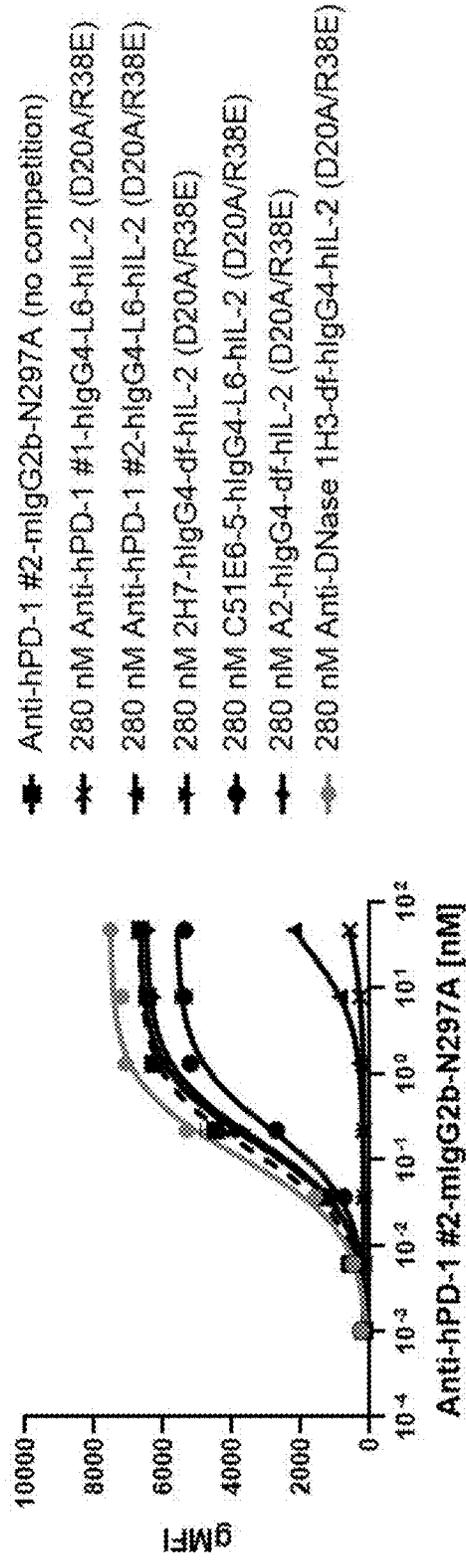


FIG. 6A



Fixed concentration of competing fusion proteins at 280 nM

FIG. 6B



Fixed concentration of competing fusion proteins at 280 nM

FIG. 7

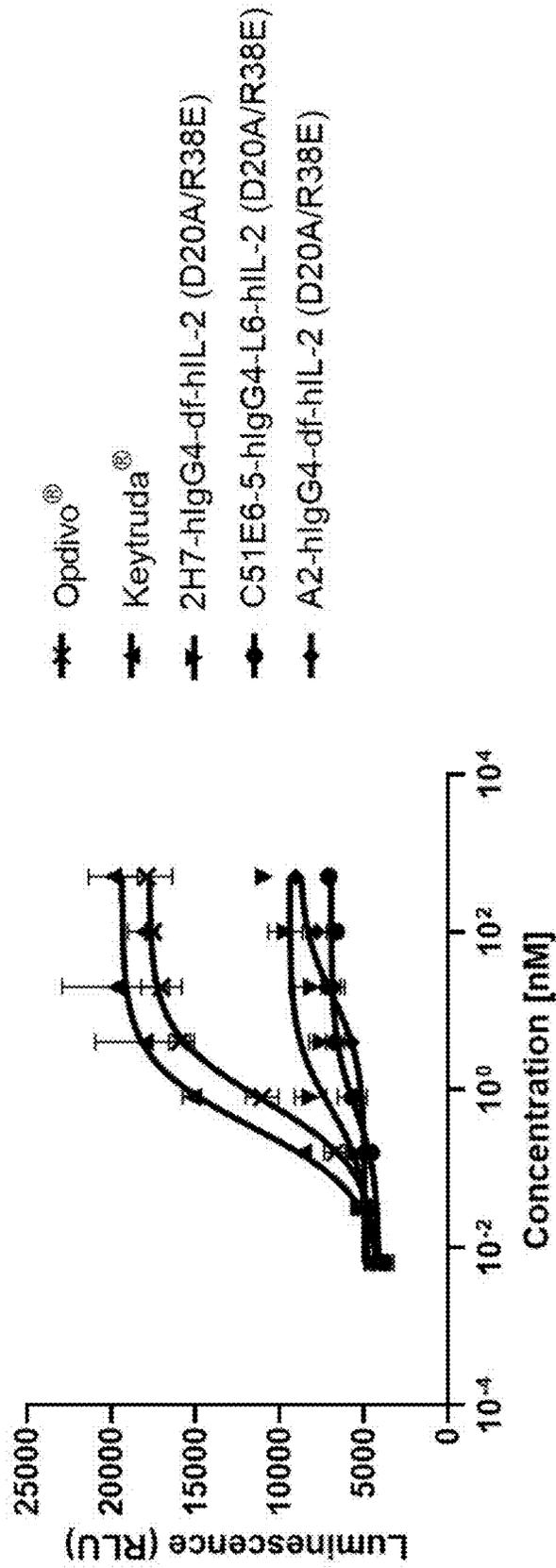


FIG. 8

MC38 colorectal solid tumor model

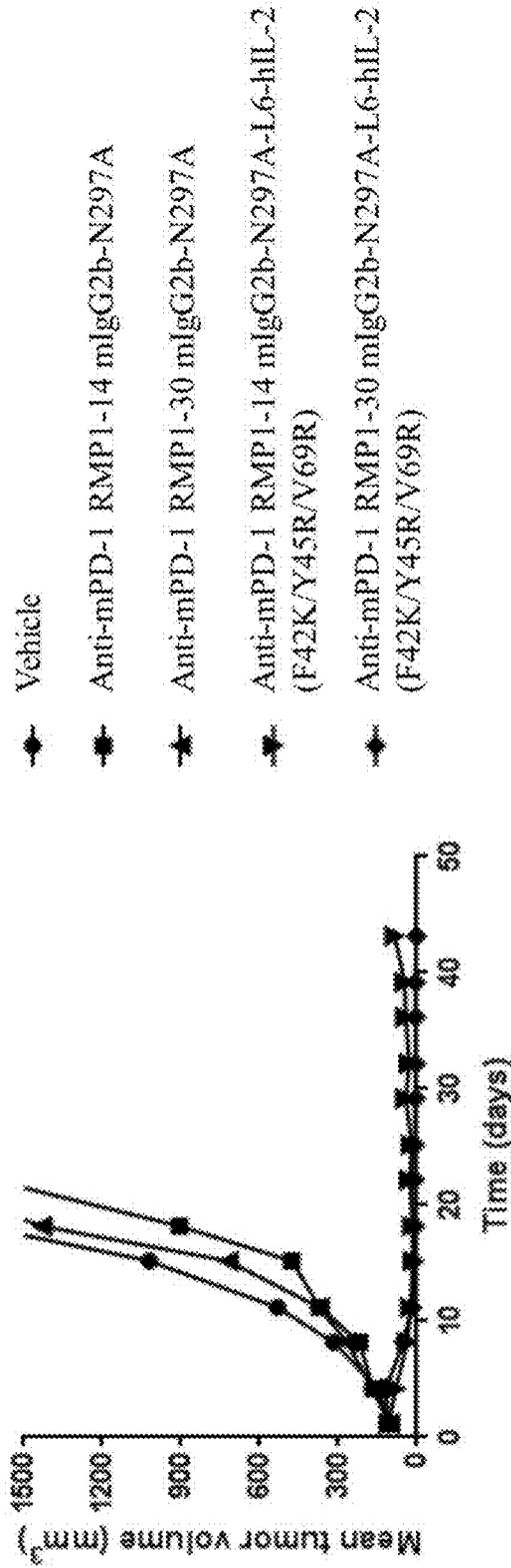


FIG. 9A

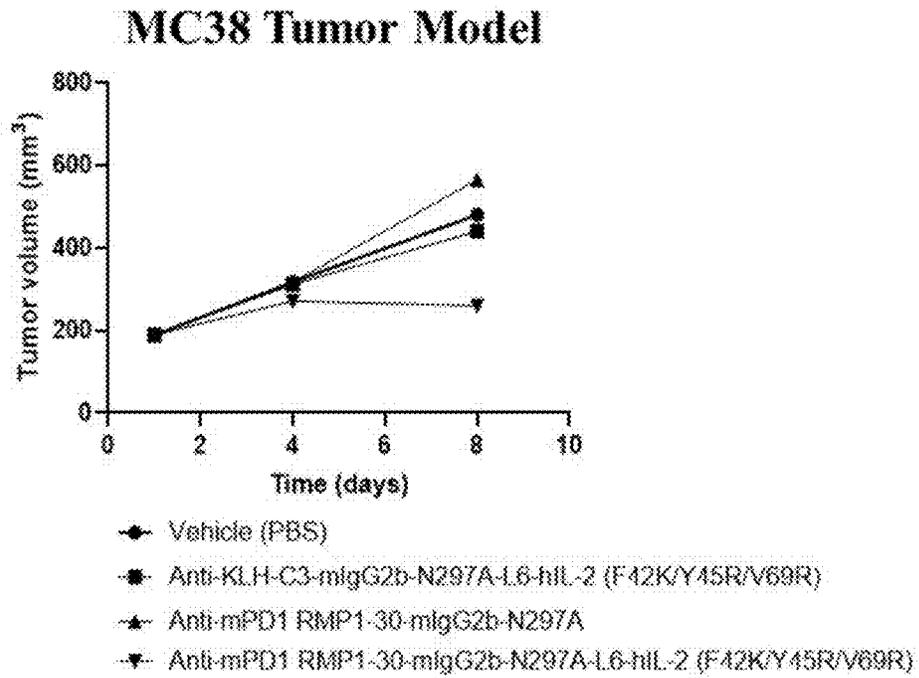


FIG. 9B

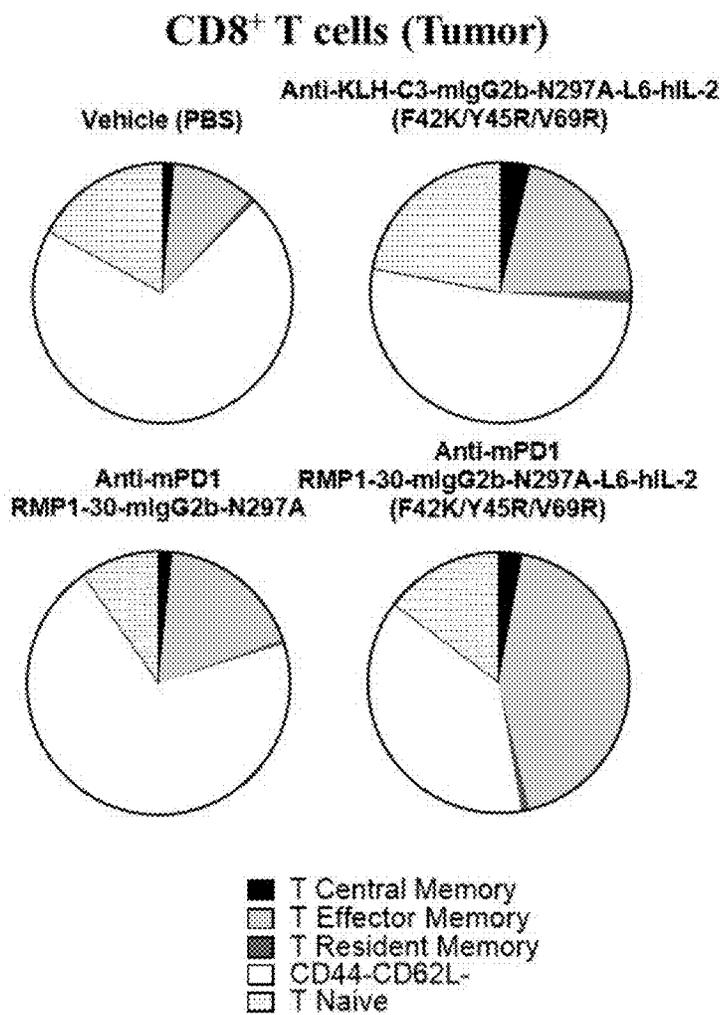
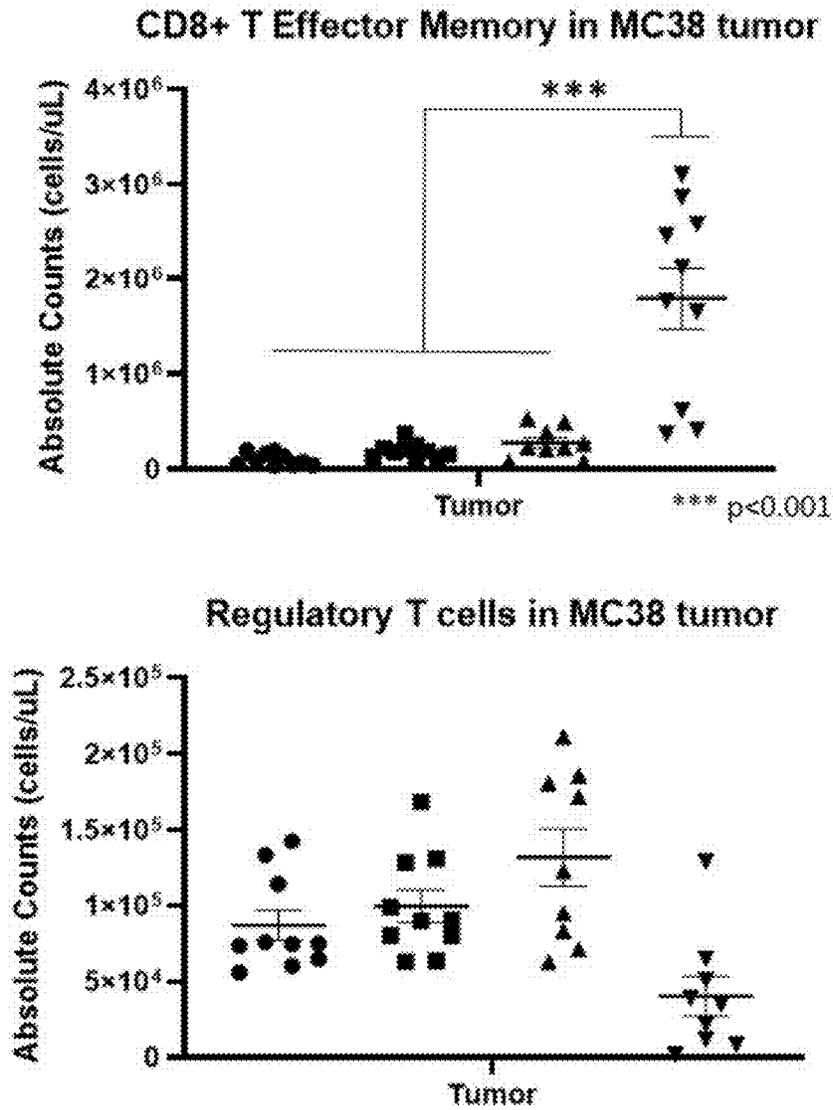


FIG. 9C



- Vehicle (PBS)
- Anti-KLH-C3-mIgG2b-N297A-L6-hIL-2 (F42K/Y45R/V69R)
- ▲ Anti-mPD1 RMP1-30-mIgG2b-N297A
- ▼ Anti-mPD1 RMP1-30-mIgG2b-N297A-L6-hIL-2 (F42K/Y45R/V69R)

FIG. 10

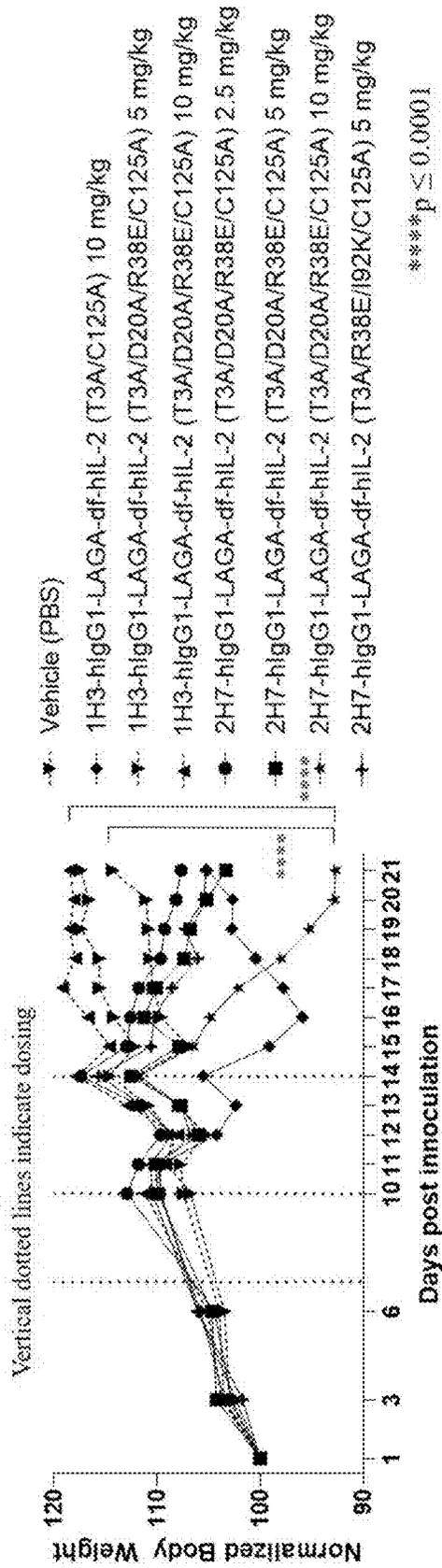


FIG. 11B

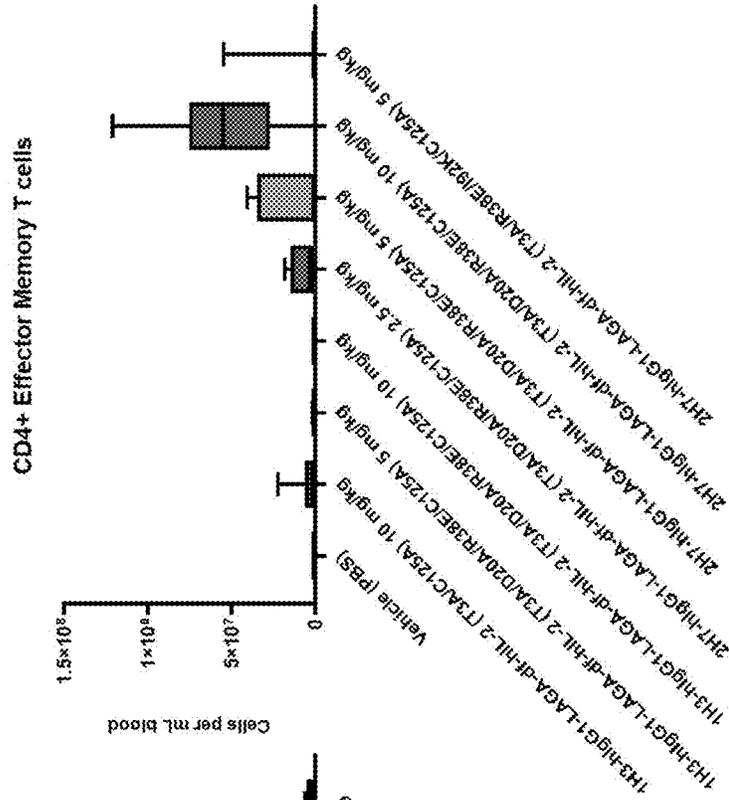


FIG. 11A

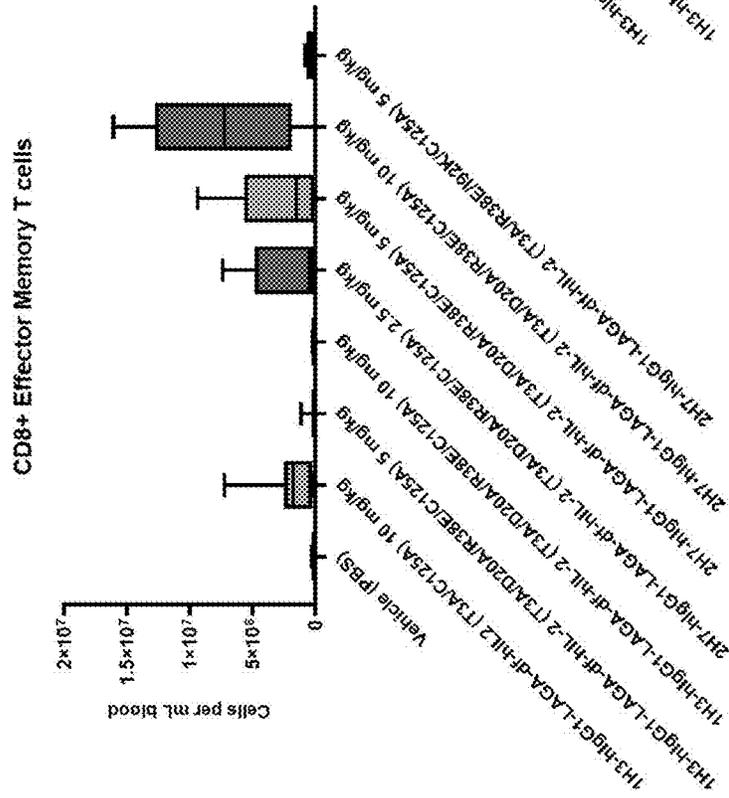


FIG. 12

Regulatory T cell (Treg) Percent of CD3⁺ T cells

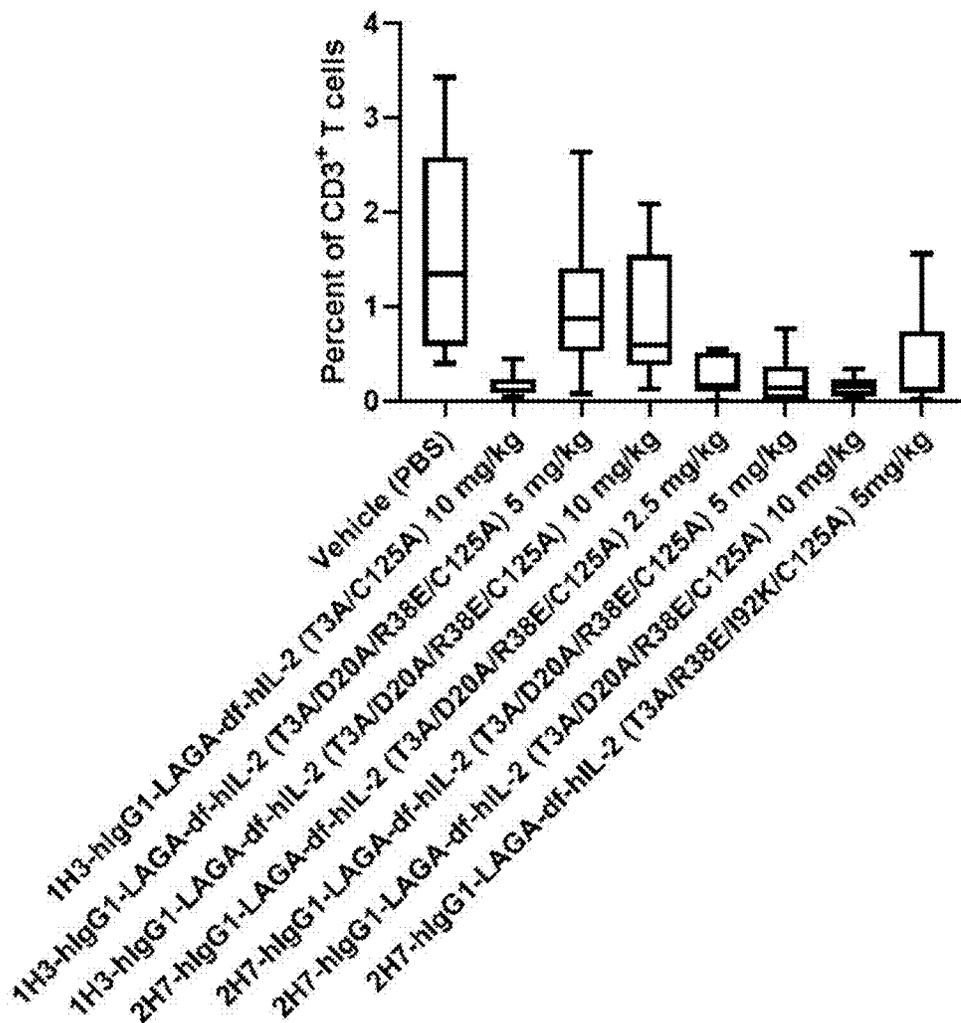


FIG. 13A

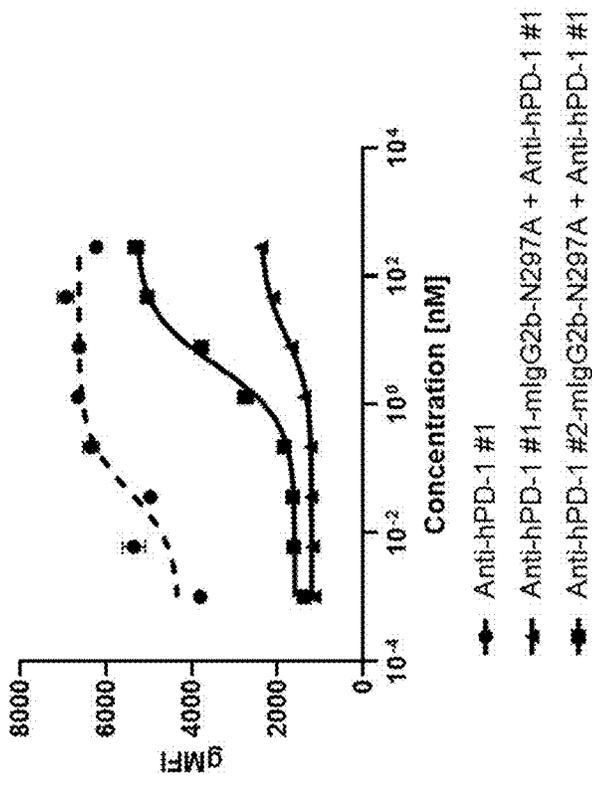


FIG. 13B

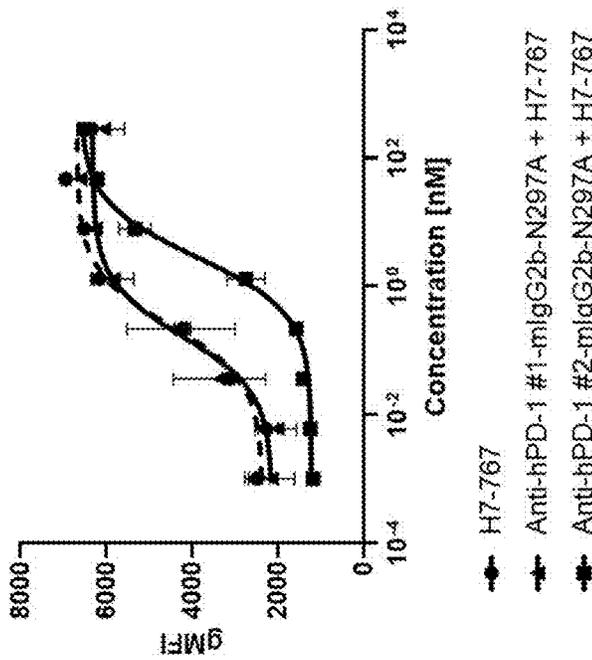


FIG. 14A

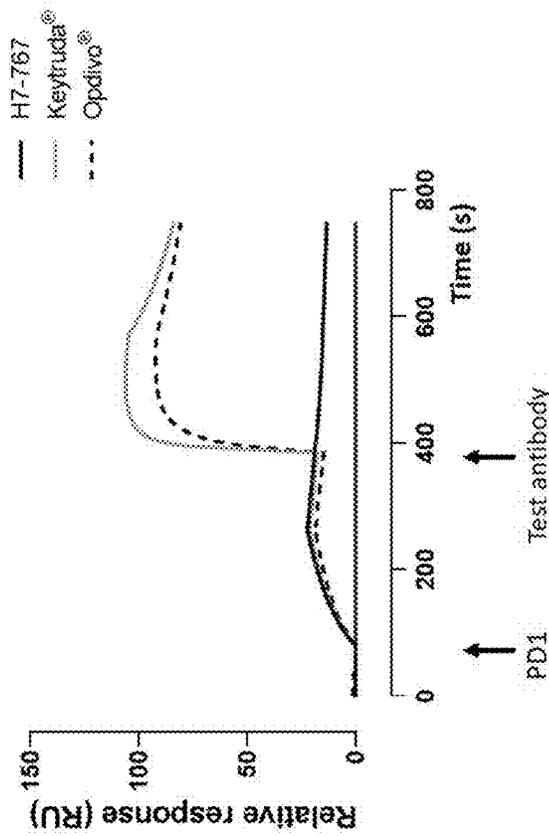
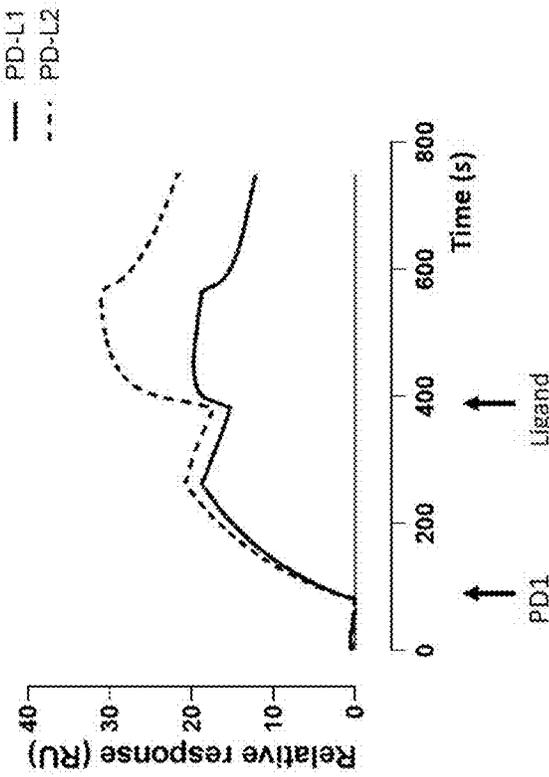


FIG. 14B



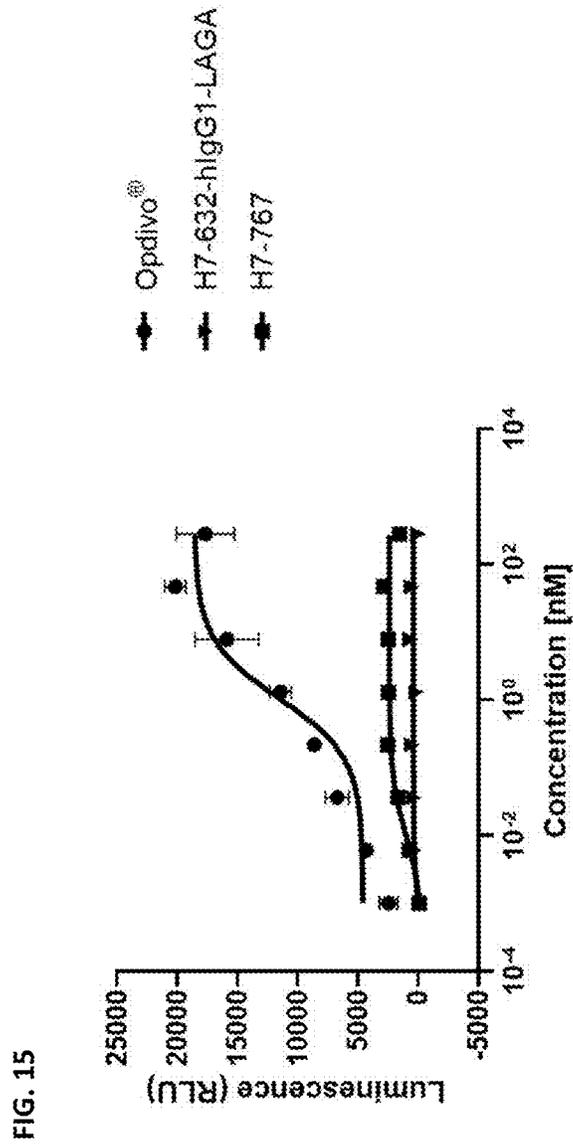


FIG. 16B

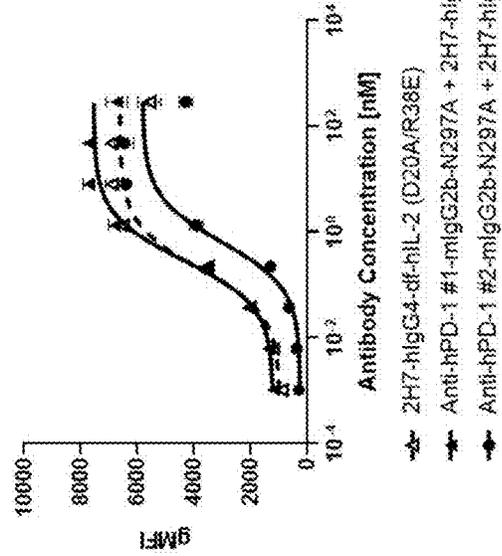


FIG. 16A

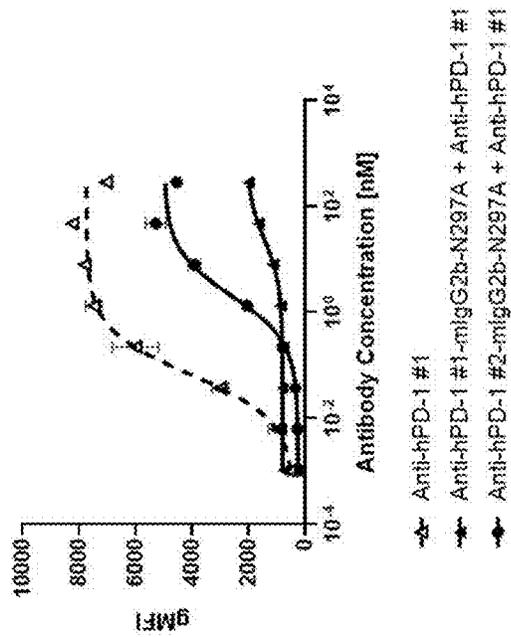


FIG. 16C

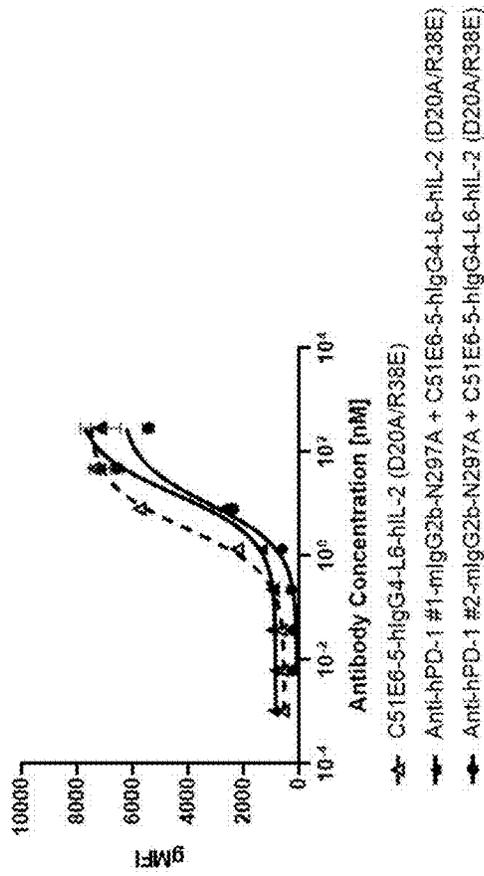
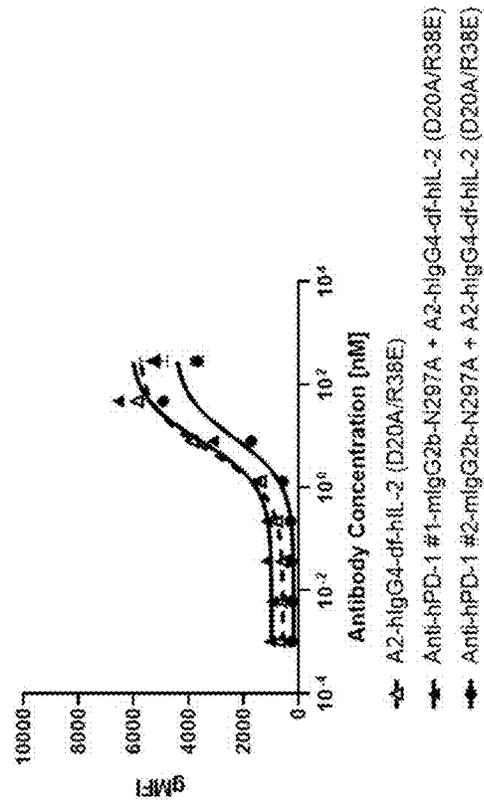


FIG. 16D



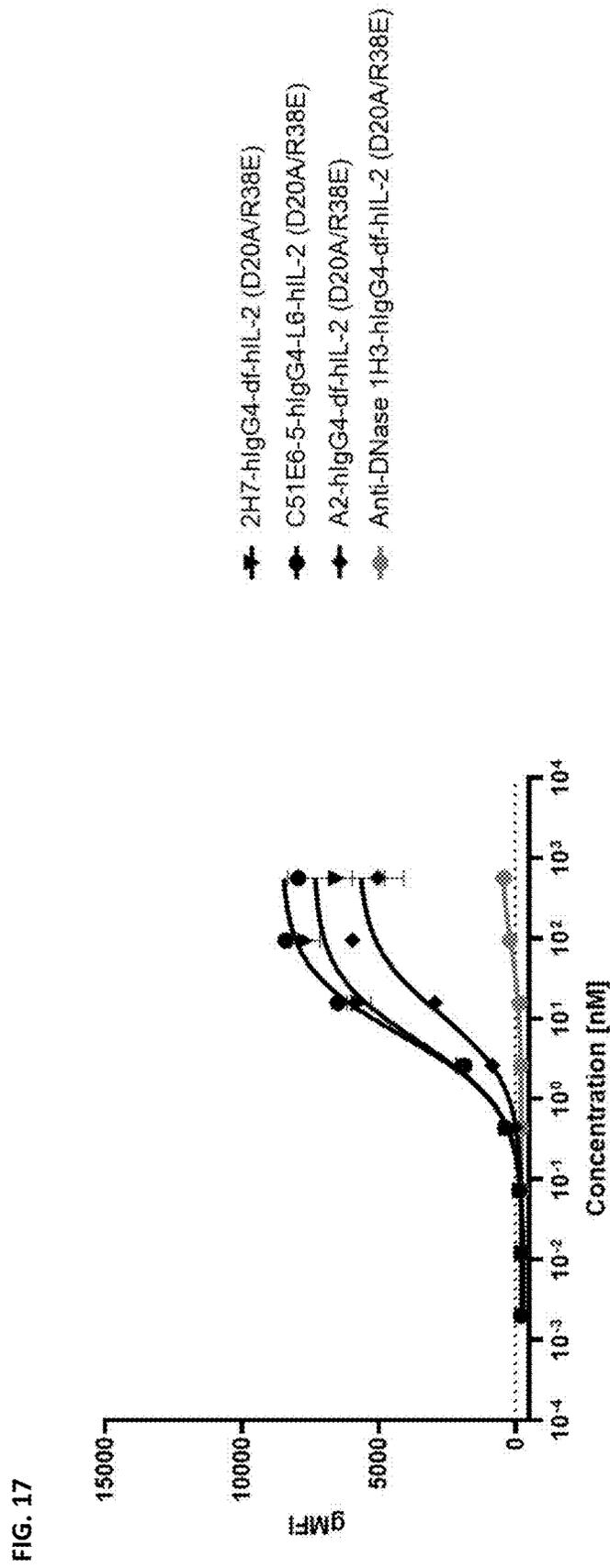


FIG. 18A

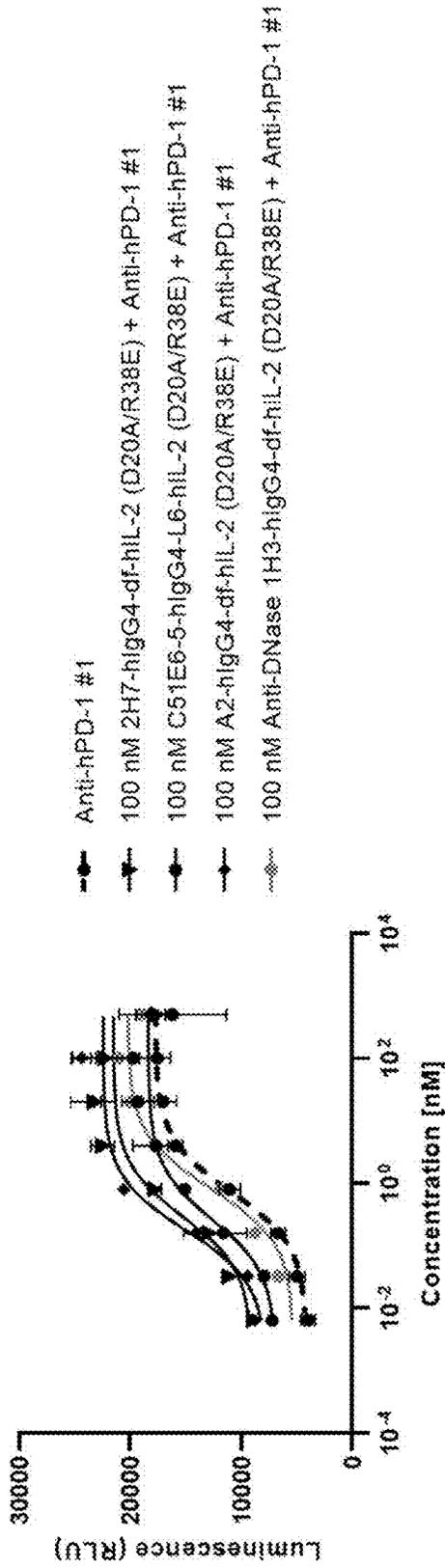


FIG. 18B

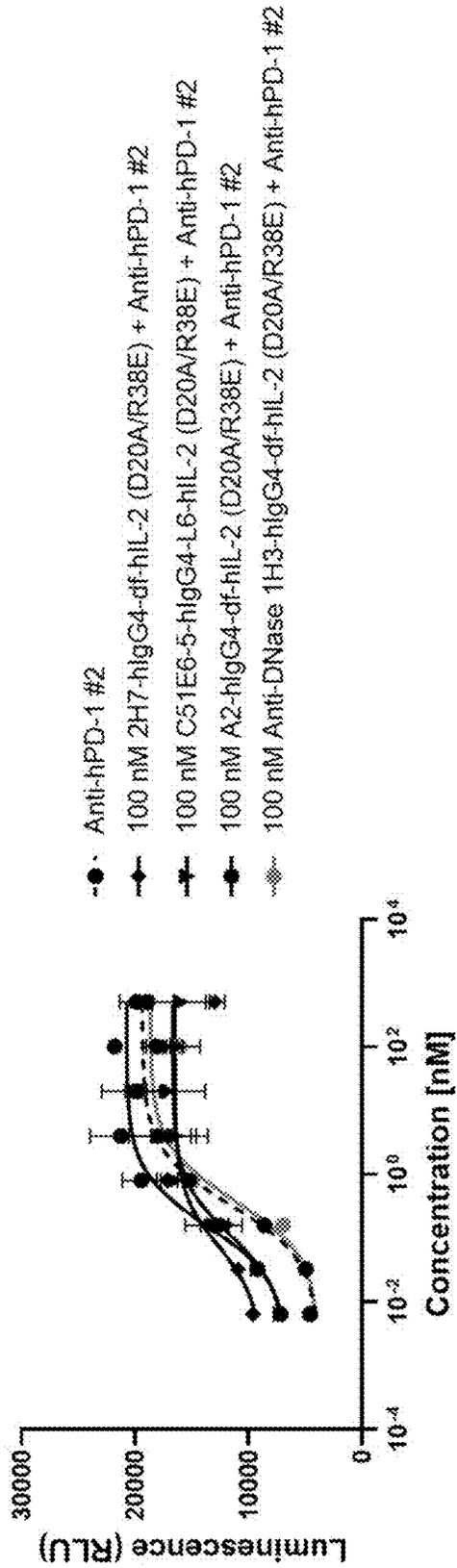


FIG. 18C

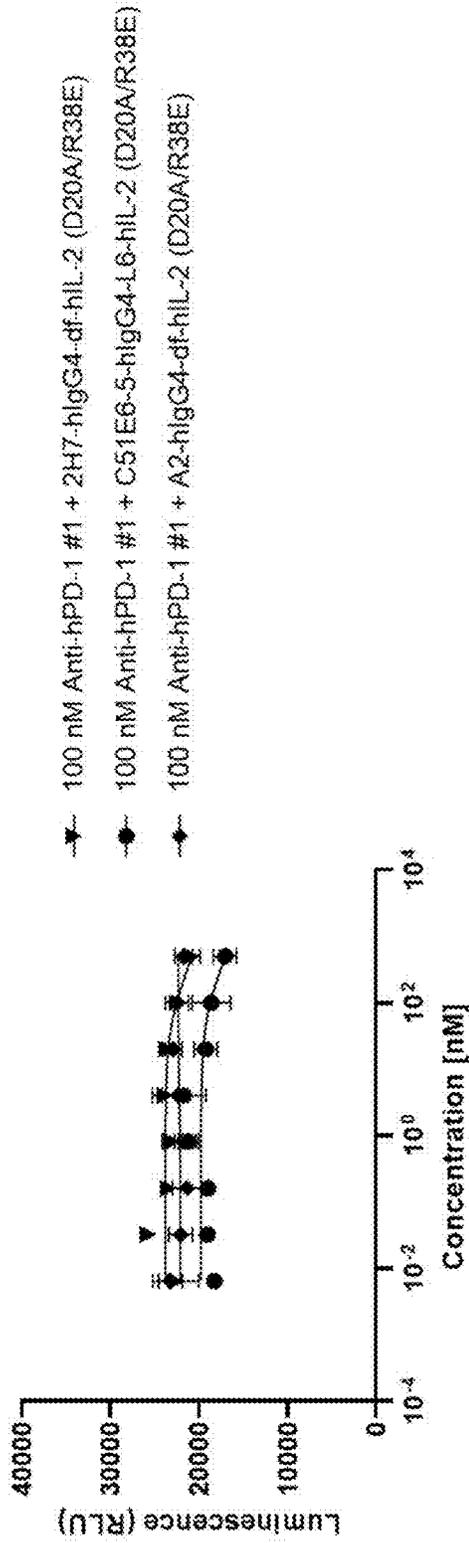
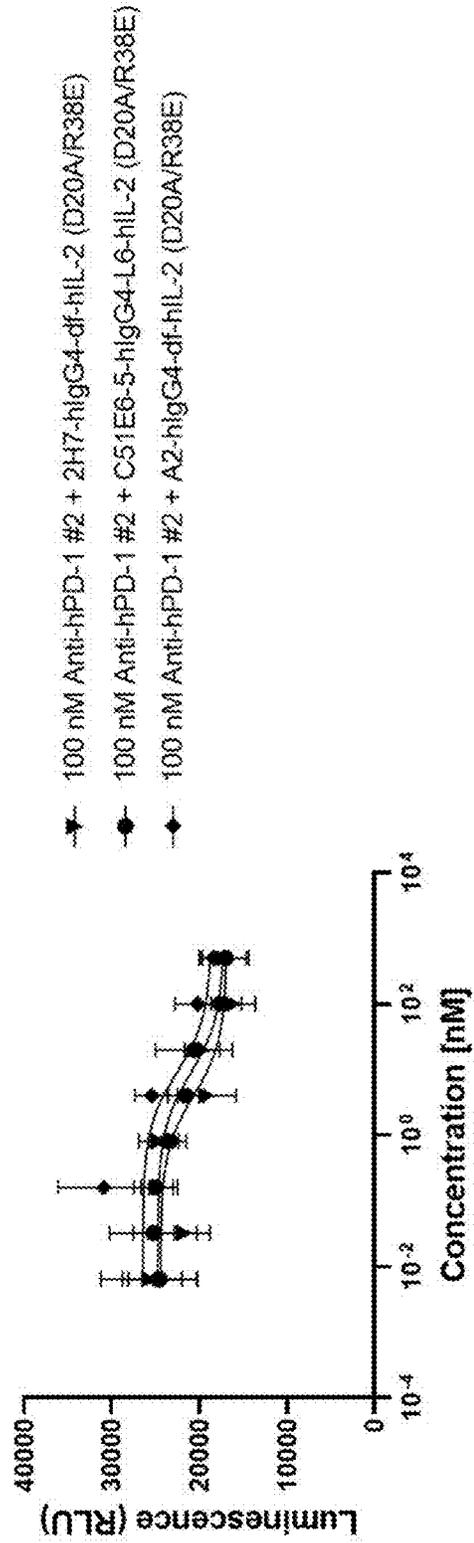


FIG. 18D



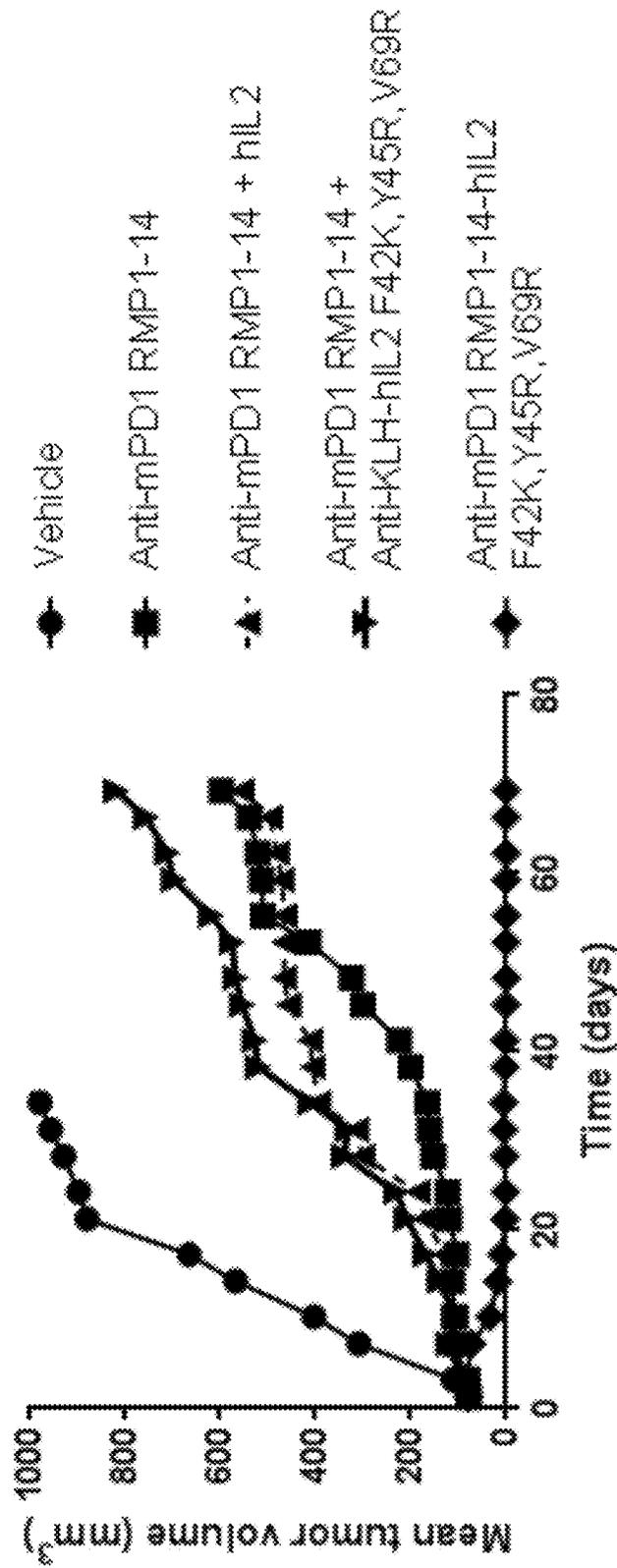


FIG. 19

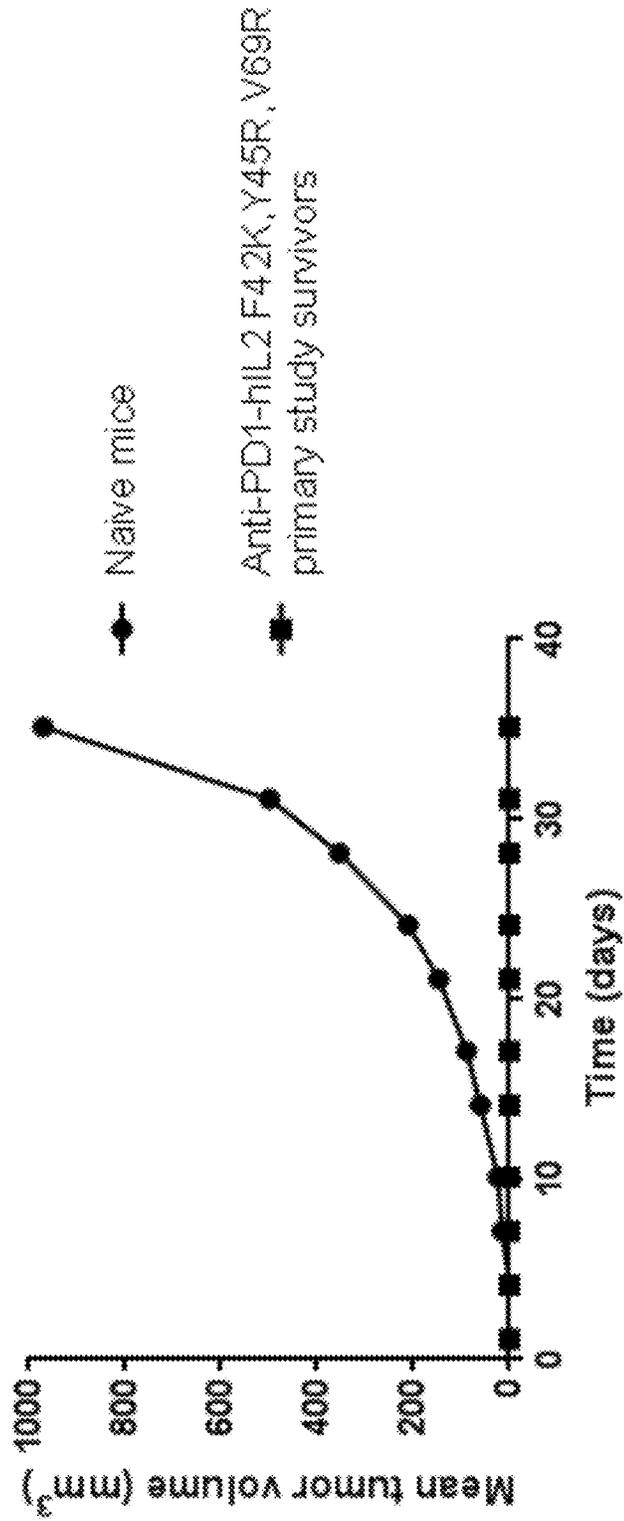


FIG. 20

1

**ANTI-PD-1 ANTIBODY-ATTENUATED IL-2
IMMUNOCONJUGATES AND USES
THEREOF**

CROSS REFERENCE TO RELATED
APPLICATIONS

This application is a continuation of U.S. application Ser. No. 18/335,650, which was filed on Jun. 15, 2023, which claims priority to U.S. Provisional Application No. 63/352,842, which was filed on Jun. 16, 2022, U.S. Provisional Application No. 63/481,630, which was filed on Jan. 26, 2023, and U.S. Provisional Application No. 63/502,746, which was filed on May 17, 2023, the disclosure of each of which are hereby incorporated by reference in their entirety.

SEQUENCE LISTING

The instant application contains a Sequence Listing which is being submitted herewith electronically in XML format and is hereby incorporated by reference in its entirety. Said XML copy, created on Aug. 26, 2024, is named 102085.002045_Sequence Listing.xml and is 696,000 bytes in size.

TECHNICAL FIELD

Disclosed herein are modified human interleukin-2 (hIL-2) proteins, human antibody molecules, or antigen-binding fragments thereof, that immunospecifically bind to human programmed cell death protein-1 (hPD-1), and immunoconjugates comprising the same.

BACKGROUND

Human IL-2 (hIL-2) is a Type 1 four α -helical bundle, glycosylated cytokine produced by CD4+ T cells and CD8+ T cells. Autocrine and paracrine IL-2 signaling occurs through engagement of either a high-affinity trimeric receptor complex comprising IL-2R α (CD25), IL-2R β (CD122), and IL-2R γ (CD132), or an intermediate-affinity dimeric receptor complex which comprises IL-2R β (CD122) and IL-2R γ (CD132). IL-2 has dual opposing and pleiotropic roles, in that it can both stimulate T cell proliferation to generate T cell effector, T cell memory, and activated NK cells, but can also stimulate suppressive regulatory T cells for maintenance of immune homeostasis. Low-dose IL-2 primarily stimulates regulatory T cells as well as some T effector and NK cells, whereas high-dose IL-2 broadly stimulates cytotoxic T cells, T effector, and NK cells and regulatory T cells. The use of IL-2 in the treatment of autoimmune diseases and as a cancer immunotherapy has, however, been limited by off-target effects and toxicity associated with the administration of IL-2.

SUMMARY

Disclosed herein are modified human interleukin-2 (hIL-2) proteins comprising a substitution at amino acid position 20 and a substitution at amino acid position 38 relative to the non-modified hIL-2 amino acid sequence of SEQ ID NO: 345, wherein the modified hIL-2 protein exhibits reduced potency on both a high affinity hIL-2 receptor and on an intermediate affinity hIL-2 receptor relative to the non-modified hIL-2.

Also disclosed herein are modified human interleukin-2 (hIL-2) proteins comprising a D20A, D20S, D20Q, D20M,

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D20I, D20V, D20N, D20G, D20T, or D20E substitution at amino acid position 20 and a R38E substitution at amino acid position 38 relative to the non-modified hIL-2 amino acid sequence of SEQ ID NO: 345.

Also disclosed herein are human antibody molecules, or antigen-binding fragments thereof, that immunospecifically bind to human programmed cell death protein-1 (hPD-1), wherein the human antibody molecule or antigen-binding fragment thereof comprises:

- a) a heavy chain complementarity determining region 1 (CDR1) comprising the amino acid sequence of SEQ ID NO: 418, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 419, a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 420, a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 421, a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 422, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 423;
- b) a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 386, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 387, a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 388, a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 389, a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 390, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 391;
- c) a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 396, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 397, a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 398, a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 399, a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 400, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 401; or
- d) a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 406, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 407, a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 408, a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 409, a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 410, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 411.

Also disclosed herein are immunoconjugates comprising:

- (a) a modified hIL-2 protein comprising a substitution at amino acid position 20 and a substitution at amino acid position 38 relative to the non-modified hIL-2 amino acid sequence of SEQ ID NO: 345; and
- (b) a human antibody molecule, or antigen-binding fragment thereof, that immunospecifically binds to hPD-1, wherein the human antibody molecule or antigen-binding fragment thereof comprises:
 - (i) a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 418, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 419, a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 420, a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 421, a light chain CDR2 comprising the amino acid

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sequence of SEQ ID NO: 422, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 423;

(ii) a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 386, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 387, a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 388, a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 389, a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 390, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 391;

(iii) a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 396, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 397, a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 398, a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 399, a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 400, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 401; or

(iv) a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 406, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 407, a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 408, a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 409, a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 410, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 411.

Pharmaceutical compositions comprising any of the herein disclosed modified hIL-2 proteins, human antibody molecules, or antigen-binding fragments thereof, or immunoconjugates are also disclosed.

Also disclosed herein are polynucleotides comprising a nucleic acid sequence encoding any of the herein disclosed modified hIL-2 proteins, human antibody molecules, or antigen-binding fragments thereof, or immunoconjugates, as well as vectors comprising the polynucleotides and transformed cells comprising the vectors.

Disclosed herein are methods of treating a disease or disorder in a subject, the methods comprising administering a therapeutically effective amount of any of the herein disclosed immunoconjugates or pharmaceutical compositions to the subject to thereby treat the disease or disorder.

Also disclosed are uses of any of the herein disclosed immunoconjugates or pharmaceutical compositions in the preparation of a medicament for the treatment of a disease, and uses of any of the herein disclosed immunoconjugates or pharmaceutical compositions for the treatment of a disease or disorder.

BRIEF DESCRIPTION OF THE DRAWINGS

The summary, as well as the following detailed description, is further understood when read in conjunction with the appended drawings. For the purpose of illustrating the disclosed modified hIL-2 proteins, anti-hPD-1 antibodies or antigen-binding fragments thereof, and immunoconjugates, there are shown in the drawings exemplary embodiments of the modified hIL-2 proteins, anti-hPD-1 antibodies or antigen-binding fragments thereof, and immunoconjugates; however, the modified hIL-2 proteins, anti-hPD-1 antibodies

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or antigen-binding fragments thereof, and immunoconjugates are not limited to the specific embodiments disclosed. In the drawings:

FIG. 1A, FIG. 1B, FIG. 1C, FIG. 1D, FIG. 1E, FIG. 1F, FIG. 1G, and FIG. 1H illustrate exemplary antibody-hIL-2 immunoconjugates as described in Example 1 herein. Non-attenuated human IL-2 cytokine (grey rectangle) was fused either directly (df) or via an L6 linker (L6) to either the N-terminus or C-terminus of both heavy chains or both kappa light chains of the antibody.

FIG. 2A, FIG. 2B, FIG. 2C, FIG. 2D, FIG. 2E, FIG. 2F, FIG. 2G, and FIG. 2H illustrate exemplary antibody-hIL-2 immunoconjugates with hCD25 (1-164) extracellular domain designed to interfere with the immunoconjugate's hIL-2 binding to the human IL-2R α . For N-terminal variants, the human CD25/IL-2R α extracellular domain (black triangle) was fused to a non-attenuated hIL-2 cytokine (grey rectangle) via an L20 linker (light grey line). Non-attenuated hIL-2 cytokine was then either directly fused (df) or fused to the antibody with an L6 linker. For C-terminal variants, the hCD25/IL-2R α extracellular domain moiety was either directly fused (df) or fused to the antibody using an L6 linker, followed by an L20 linker and non-attenuated hIL-2 cytokine.

FIG. 3 illustrates an exemplary 1H3-hIgG1-L6-hIL-2 immunoconjugate that contains a CD25/IL-2R α extracellular domain moiety. The hCD25/IL-2R α extracellular domain moiety was fused to the 1H3-hIgG1-L6-hIL-2 at the C-terminus of each heavy chain via an L6 linker followed by an L20 linker and hIL-2 cytokine moiety containing substitutions predicted to modulate binding to CD122/IL-2R β as described in Example 2 (attenuated hIL-2).

FIG. 4A, FIG. 4B, FIG. 4C, and FIG. 4D show the results of experiments analyzing the binding of the anti-hPD-1 antibodies 2H7-hIgG4, C51E6-5-hIgG4, and A2-hIgG4 to the human PD-1 receptor on Jurkat cells in the presence of saturating concentrations of anti-hPD-1 #1-mIgG2b-N297A and anti-hPD-1 #2-mIgG2b-N297A (10 μ M) prior to exposure with anti-hPD-1 antibodies.

FIG. 5 illustrates exemplary anti-hPD-1-attenuated hIL-2 immunoconjugates either with an L6 linker (L6) (left) or direct fusion (df) (right). Anti-hPD-1 antibodies comprising either hIgG4 or hIgG1 Fc domains, with or without L235E (LE) or L235A/G237A (LAGA) modifications in the Fc domain, were fused to attenuated hIL-2 cytokines at the C-terminus of the antibody heavy chains. Various substitutions in the hIL-2 cytokine were introduced for potency attenuation.

FIG. 6A and FIG. 6B show the results of competition assays demonstrating that anti-hPD-1 #1-mIgG2b-N297A (FIG. 6A) or anti-hPD-1 #2-mIgG2b-N297A (FIG. 6B) bind to anti-hPD-1 receptor on Jurkat cells in the presence of saturating concentrations of anti-hPD-1-attenuated hIL-2 immunoconjugates (280 nM).

FIG. 7 shows the results of competition assays demonstrating that the anti-hPD-1-attenuated hIL-2 immunoconjugates 2H7-hIgG4-df-hIL-2 (D20A/R38E), C51E6-5-L6-hIgG4-hIL-2 (D20A/R38E), and A2-hIgG4-df-hIL-2 (D20A/R38E) do not inhibit the binding of human PD-L1 to the human PD-1 receptor using the PD-1/PD-L1 Blockade Bioassay.

FIG. 8 shows the results of experiments analyzing the effect of the administration of vehicle, surrogate anti-PD-1 antibodies (anti-mPD-1 RMP1-14 mIgG2b-N297A and anti-mPD-1 RMP1-30 mIgG2b-N297A), and surrogate anti-PD-1-attenuated hIL-2 immunoconjugates (anti-mPD-1 RMP1-14 mIgG2b-N297A-L6-hIL-2 (F42K/Y45R/V69R) or anti-

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mPD-1 RMP1-30 mIgG2b-N297A-L6-hIL-2 (F42K/Y45R/V69R)) on the growth of established subcutaneous MC38 syngeneic tumors in C57BL/6 mice, as described in Example 18. Test agents were dosed intraperitoneally at 5 mg/kg twice weekly for 4 weeks, starting on day 1. The points on the graph represent mean tumor volumes of an average of 10 mice per group.

FIG. 9A, FIG. 9B, and FIG. 9C illustrate the results of studies conducted to determine the efficacy of surrogate anti-hPD-1-attenuated hIL-2 immunoconjugate anti-mPD-1 RMP1-30 mIgG2b-N297A-hIL-2 (F42K/Y45R/V69R) in an MC38 murine colon adenocarcinoma model. FIG. 9A depicts the mean subcutaneous tumor volumes (mm³) measured every 3-4 days for 8 days after the first dose of test agents (3 doses on days 1, 4, and 8 at 5 mg/kg). Tumor growth curves represent an average of 15 animals per group. FIG. 9B summarizes results from immunophenotyping tumors by flow cytometry on day 9, showing the proportion of different CD8⁺ T cell subsets as fractions of the total CD8⁺ T cell average absolute counts. FIG. 9C illustrates immunophenotyping results on day 9 which demonstrated that there was a significant expansion of CD8⁺ T effector memory and a trend towards decreased regulatory T cells in tumors (cells/ μ L) following exposure to the surrogate immunoconjugate.

FIG. 10 shows the results from an experiment analyzing the acceleration of Graft vs Host Disease in NOD-Prkdc^{em26Cd52}IL-2rg^{em26Cd22}/NjuCrI (NCG) mice exposed to anti-hPD-1-attenuated hIL-2 immunoconjugates, as demonstrated by significant body weight decrease in an NCG-PBMC model.

FIG. 11A and FIG. 11B show the results of an experiment analyzing the dose-dependent expansion of cells/mL of blood CD8⁺ Effector Memory T cells (FIG. 11A) and CD4⁺ Effector Memory T cells (FIG. 11B) of NOD-Prkdc^{em26Cd2}IL-2rg^{em26Cd22}/NjuCrI (NCG) mice treated with 2H7-hIgG1-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) in the NCG-PBMC model.

FIG. 12 shows a decrease in cells/mL of blood regulatory T cells of NOD-Prkdc^{em26Cd52}IL-2rg^{em26Cd22}/NjuCrI (NCG) mice treated with 2H7-hIgG1-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) in the NCG-PBMC model.

FIG. 13A and FIG. 13B show that H7-632-hIgG1-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) (designated "H7-767") (FIG. 13B) continues to bind to the human PD-1 receptor on Jurkat cells in the presence of saturating concentrations of anti-hPD-1 #1-mIgG2b-N297A and anti-hPD-1 #2-mIgG2b-N297A (10 μ M) prior to exposure.

FIG. 14A and FIG. 14B are graphs showing the binding of recombinant human PD-1 captured by H7-767 immobilized to a CM5 sensor chip followed by binding of either (FIG. 14A) H7-767, KEYTRUDA®, or OPDIVO® or (FIG. 14B) PD-L1 or PD-L2, as evaluated by surface plasmon resonance (SPR).

FIG. 15 demonstrates that H7-632-hIgG1-LAGA and H7-767 do not inhibit the binding of human PD-L1 to the human PD-1 receptor using an hPD-1/hPD-L1 Blockade Bioassay.

FIG. 16A, FIG. 16B, FIG. 16C, and FIG. 16D are graphs showing the binding of anti-hPD-1-attenuated hIL-2 immunoconjugates 2H7-hIgG4-df-hIL-2 (D20A/R38E), C51E6-5-hIgG4-df-hIL-2 (D20A/R38E), and A2-hIgG4-df-hIL-2 (D20A/R38E) to the human PD-1 receptor on Jurkat cells in the presence of saturating concentrations of anti-hPD-1 #1-mIgG2b-N297A and anti-hPD-1 #2-mIgG2b-N297A (10 μ M) prior to exposure with anti-hPD-1-attenuated hIL-2 immunoconjugates, as assessed by flow cytometry.

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FIG. 17 is a graph showing the binding of 2H7-hIgG4-df-hIL-2 (D20A/R38E), C51E6-5-hIgG4-df-hIL-2 (D20A/R38E), A2-hIgG4-df-hIL-2 (D20A/R38E) and the irrelevant antibody control 1H3-hIgG4-df-hIL-2 (D20A/R38E) to HEK-293T cells recombinantly expressing cynomolgus PD-1, as assessed by flow cytometry.

FIG. 18A, FIG. 18B, FIG. 18C, and FIG. 18D show the antagonist activity of anti-hPD-1-attenuated hIL-2 immunoconjugates 2H7-hIgG4-df-hIL-2 (D20A/R38E), C51E6-5-hIgG4-df-hIL-2 (D20A/R38E), and A2-hIgG4-df-hIL-2 (D20A/R38E) in the presence of anti-hPD-1 #1 or anti-hPD-1 #2. FIG. 18A and FIG. 18B show results from the titration of anti-hPD-1 #1 or anti-hPD-1 #2 in the presence of fixed concentration anti-hPD-1-attenuated hIL-2 immunoconjugates. FIG. 18C and FIG. 18D show the results from the converse experiment in which anti-hPD-1-attenuated hIL-2 immunoconjugates were titrated with a fixed concentration of 100 nM of anti-hPD-1 #1 (FIG. 18C) or 100 nM of anti-hPD-1 #2 (FIG. 18D).

FIG. 19 shows the effect of the administration of various test agents including a surrogate anti-mouse PD-1/attenuated IL-2 immunoconjugate on the growth of established subcutaneous MC38 syngeneic tumors in C57BL/6 mice. Each growth curve represents the mean tumor volume of ten mice per treatment group.

FIG. 20 shows the ability of MC38 tumor cells to grow in tumor naïve mice compared to mice from the MC38 primary tumor study illustrated in FIG. 19 that were previously dosed with anti-mPD-1-hIL-2 F42K/Y45R/V69R and which had demonstrated complete long-term regression of the established primary tumor. Animals from both cohorts (10 mice per group) were subcutaneously implanted with 5 \times 10⁵ MC38 tumor cells on the left flank contralateral to the location of the primary tumor. Mice previously exposed to the surrogate agent anti-mPD-1-hIL-2 F42K/Y45R/V69R demonstrated no tumor growth as they had developed a sustained immunity, whilst corresponding naïve mice controls demonstrated the typical growth of tumors in their flanks.

DETAILED DESCRIPTION OF ILLUSTRATIVE EMBODIMENTS

The disclosed modified hIL-2 proteins, human antibody molecules or antigen-binding fragments thereof, and immunoconjugates may be understood more readily by reference to the following detailed description taken in connection with the accompanying figures, which form a part of this disclosure. It is to be understood that the disclosed modified hIL-2 proteins, human antibody molecules or antigen-binding fragments thereof, and immunoconjugates described and/or shown herein, and that the terminology used herein is for the purpose of describing particular embodiments by way of example only and is not intended to be limiting of the claimed modified hIL-2 proteins, human antibody molecules or antigen-binding fragments thereof, and immunoconjugates.

Unless specifically stated otherwise, any description as to a possible mechanism or mode of action or reason for improvement is meant to be illustrative only, and the disclosed modified hIL-2 proteins, human antibody molecules or antigen-binding fragments thereof, and immunoconjugates are not to be constrained by the correctness or incorrectness of any such suggested mechanism or mode of action or reason for improvement.

Throughout this text, the descriptions refer to modified hIL-2 proteins, human antibody molecules or antigen-binding fragments thereof, and immunoconjugates, as well as methods of using the modified hIL-2 proteins, human antibody molecules or antigen-binding fragments thereof, and immunoconjugates. Where the disclosure describes or claims a feature or embodiment associated with a modified hIL-2 protein, human antibody molecule or antigen-binding fragment thereof, and immunoconjugate, such a feature or embodiment is equally applicable to the methods of using the modified hIL-2 proteins, human antibody molecules or antigen-binding fragments thereof, and immunoconjugates. Likewise, where the disclosure describes or claims a feature or embodiment associated with a method of using a modified hIL-2 protein, human antibody molecule or antigen-binding fragment thereof, and immunoconjugate, such a feature or embodiment is equally applicable to the modified hIL-2 proteins, human antibody molecules or antigen-binding fragments thereof, and immunoconjugates.

Where a range of numerical values is recited or established herein, the range includes the endpoints thereof and all the individual integers and fractions within the range, and also includes each of the narrower ranges therein formed by all the various possible combinations of those endpoints and internal integers and fractions to form subgroups of the larger group of values within the stated range to the same extent as if each of those narrower ranges was explicitly recited. Where a range of numerical values is stated herein as being greater than a stated value, the range is nevertheless finite and is bounded on its upper end by a value that is operable within the context of the herein disclosure. Where a range of numerical values is stated herein as being less than a stated value, the range is nevertheless bounded on its lower end by a non-zero value. It is not intended that the scope of the modified hIL-2 proteins, human antibody molecules or antigen-binding fragments thereof, and immunoconjugates be limited to the specific values recited when defining a range. All ranges are inclusive and combinable.

When values are expressed as approximations, by use of the antecedent "about," it will be understood that the particular value forms another embodiment. Reference to a particular numerical value includes at least that particular value, unless the context clearly dictates otherwise. The term "about" when used in reference to numerical ranges, cutoffs, or specific values is used to indicate that the recited values may vary by up to as much as 10% from the listed value. Thus, the term "about" is used to encompass variations of +10% or less, variations of +5% or less, variations of +1% or less, variations of +0.5% or less, or variations of +0.1% or less from the specified value.

It is to be appreciated that certain features of the disclosed modified hIL-2 proteins, human antibody molecules or antigen-binding fragments thereof, and immunoconjugates which are, for clarity, described herein in the context of separate embodiments, may also be provided in combination in a single embodiment. Conversely, various features of the disclosed modified hIL-2 proteins, human antibody molecules or antigen-binding fragments thereof, and immunoconjugates that are, for brevity, described in the context of a single embodiment, may also be provided separately or in any subcombination.

As used herein, the singular forms "a," "an," and "the" include the plural.

Various terms relating to aspects of the description are used throughout the specification and claims. Such terms are to be given their ordinary meaning in the art unless other-

wise indicated. Other specifically defined terms are to be construed in a manner consistent with the definitions provided herein.

The term "comprising" is intended to include examples encompassed by the terms "consisting essentially of" and "consisting of"; similarly, the term "consisting essentially of" is intended to include examples encompassed by the term "consisting of."

The term "antibody molecule" is meant in a broad sense and includes full length immunoglobulin molecules and antigen-binding fragments thereof.

Immunoglobulins can be assigned to five major classes, namely IgA, IgD, IgE, IgG, and IgM, depending on the heavy chain constant domain amino acid sequence. IgA and IgG are further sub-classified as the isotypes IgA1, IgA2, IgG1, IgG2, IgG3, and IgG4. Antibody light chains of any vertebrate species can be assigned to one of two clearly distinct types, namely kappa (κ) and lambda (λ), based on the amino acid sequences of their constant domains.

"Antigen-binding fragment" refers to a portion of an immunoglobulin molecule that retains the antigen binding properties of the parental full length antibody (i.e., "antigen-binding fragment thereof"). Exemplary antigen binding fragments can have: heavy chain complementarity determining regions (CDR) 1, 2, and/or 3; light chain CDR1, 2, and/or 3; a heavy chain variable region (VH); a light chain variable region (VL); and combinations thereof. Antigen binding fragments include: a Fab fragment, a monovalent fragment consisting of the VL, VH, constant light (CL), and constant heavy 1 (CH1) domains; a F(ab)2 fragment, a bivalent fragment comprising two Fab fragments linked by a disulfide bridge at the hinge region; a Fd fragment consisting of the VH and CH1 domains; a Fv fragment consisting of the VL and VH domains of a single arm of an antibody; and a domain antibody (dAb) fragment (Ward et al., Nature 341:544-546, 1989), which consists of a VH domain or a VL domain. VH and VL domains can be engineered and linked together via a synthetic linker to form various types of single chain antibody designs where the VH/VL domains pair intramolecularly, or intermolecularly in those cases when the VH and VL domains are expressed by separate single chain antibody constructs, to form a monovalent antigen binding site, such as single chain Fv (scFv) or diabody, described for example in Int'l Pat. Pub. Nos. WO1998/44001, WO1988/01649, WO1994/13804, and WO1992/01047. These antibody fragments are obtained using techniques well known to those of skill in the art, and the fragments are screened for utility in the same manner as are full length antibodies.

The phrase "immunospecifically binds" refers to the ability of the disclosed antibody molecules to preferentially bind to its target (hPD-1 in the case of anti-hPD-1 antibody molecules) without preferentially binding other molecules in a sample containing a mixed population of molecules. Antibody molecules that immunospecifically bind hPD-1 are substantially free of other antibodies having different antigenic specificities (e.g., an anti-hPD-1 antibody is substantially free of antibodies that specifically bind antigens other than hPD-1). Antibody molecules that immunospecifically bind hPD-1, however, can have cross-reactivity to other antigens, such as orthologs of hPD-1, including *Macaca fascicularis* (cynomolgus monkey) PD-1. The antibody molecules disclosed herein are able to immunospecifically bind both naturally-produced hPD-1 and to PD-1 which is recombinantly produced in mammalian or prokaryotic cells.

An antibody variable region consists of four “framework” regions interrupted by three “antigen binding sites.” The antigen binding sites are defined using various terms: (i) Complementarity Determining Regions (CDRs), three in the VH (HCDR1, HCDR2, HCDR3), and three in the VL (LCDR1, LCDR2, LCDR3) are based on sequence variability (Wu and Kabat *J Exp Med* 132:211-50, 1970; Kabat et al., *Sequences of Proteins of Immunological Interest*, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, Md., 1991); and (ii) “Hypervariable regions” (“HVR” or “HV”), three in the VH (H1, H2, H3) and three in the VL (L1, L2, L3) refer to the regions of the antibody variable domains which are hypervariable in structure as defined by Chothia and Lesk (Chothia and Lesk *Mol Biol* 196:901-17, 1987). The AbM definition of CDRs is also widely used; it is a compromise between Kabat and Chothia numbering schemes and is so-called because it was used by Oxford Molecular’s AbM antibody modelling software (Rees, A. R., Searle, S. M. J., Henry, A. H. and Pedersen, J. T. (1996) In Sternberg M. J. E. (ed.), *Protein Structure Prediction*. Oxford University Press, Oxford, 141-172). Other terms include “IMGT-CDRs” (Lefranc et al., *Dev Comparat Immunol* 27:55-77, 2003) and “Specificity Determining Residue Usage” (SDRU) (Almagro *Mol Recognit* 17:132-43, 2004). The International Immunogenetics (IMGT) database ([http://www_imgt_org](http://www.imgt.org)) provides a standardized numbering and definition of antigen-binding sites. The correspondence between CDRs, HVs and IMGT delineations is described in Lefranc et al., *Dev Comparat Immunol* 27:55-77, 2003.

“Framework” or “framework sequences” are the remaining sequences of a variable region other than those defined to be antigen binding sites. Because the antigen binding sites can be defined by various terms as described above, the exact amino acid sequence of a framework depends on how the antigen-binding site was defined.

“Human antibody,” “fully human antibody,” and like terms refers to an antibody having heavy and light chain variable regions in which both the framework and the antigen binding sites are derived from sequences of human origin. If the antibody contains a constant region, the constant region also is derived from sequences of human origin. A human antibody comprises heavy and/or light chain variable regions that are “derived from” sequences of human origin if the variable regions of the antibody are obtained from a system that uses human germline immunoglobulin or rearranged immunoglobulin genes. Such systems include human immunoglobulin gene libraries displayed on phage, and transgenic non-human animals such as mice or chicken carrying human immunoglobulin loci as described herein. “Human antibody” may contain amino acid differences when compared to the human germline or rearranged immunoglobulin sequences due to, for example, naturally occurring somatic mutations or intentional introduction of substitutions in the variable domain (framework and antigen binding sites), or constant domain. Typically, a “human antibody” is at least about 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical in amino acid sequence to an amino acid sequence encoded by a human germline or rearranged immunoglobulin gene. In some cases, a “human antibody” may contain consensus framework sequences derived from human framework sequence analyses, for example as described in Knappik et al., *J Mol Biol* 296:57-86, 2000, or synthetic HCDR3 incorporated into human immunoglobulin gene libraries displayed on phage, as described in, for example, Shi et al., *J Mol Biol*

397:385-96, 2010 and Int’l Pat. Pub. No. WO2009/085462. Antibodies in which antigen binding sites are derived from a non-human species are not included in the definition of “human antibody.”

Human antibodies, while derived from human immunoglobulin sequences, may be generated using systems such as phage display incorporating synthetic CDRs and/or synthetic frameworks, or can be subjected to *in vitro* mutagenesis to improve antibody properties in the variable regions or the constant regions or both, resulting in antibodies that do not naturally exist within the human antibody germline repertoire *in vivo*.

“Recombinant antibody” includes all antibodies that are prepared, expressed, created, or isolated by recombinant means, such as: antibodies isolated from an animal (e.g., a mouse) that is transgenic or transchromosomal for human immunoglobulin genes or a hybridoma prepared therefrom (described further below); antibodies isolated from a host cell transformed to express the antibody; antibodies isolated from a recombinant, combinatorial antibody library; and antibodies prepared, expressed, created, or isolated by any other means that involve splicing of human immunoglobulin gene sequences to other DNA sequences, or antibodies that are generated *in vitro* using Fab arm exchange.

“Monoclonal antibody” refers to a population of antibody molecules of a single molecular composition. A monoclonal antibody composition displays a single binding specificity and affinity for a particular epitope, or in a case of a bispecific monoclonal antibody, a dual binding specificity to two distinct epitopes. Monoclonal antibody therefore refers to an antibody population with single amino acid composition in each heavy and each light chain, except for possible well known alterations such as removal of C-terminal lysine from the antibody heavy chain. Monoclonal antibodies may have heterogeneous glycosylation within the antibody population. Monoclonal antibody may be monospecific or multispecific, or monovalent, bivalent or multivalent. A bispecific antibody is included in the term monoclonal antibody.

“Epitope” refers to a portion of an antigen to which an antibody specifically binds. Epitopes usually consist of chemically active (such as polar, non-polar, or hydrophobic) surface groupings of moieties such as amino acids or polysaccharide side chains and can have specific three-dimensional structural characteristics, as well as specific charge characteristics. An epitope can be composed of contiguous and/or discontinuous amino acids that form a conformational spatial unit. For a discontinuous epitope, amino acids from differing portions of the linear sequence of the antigen come in close proximity in 3-dimensional space through the folding of the protein molecule.

“Variant” refers to a polypeptide or a polynucleotide that differs from a reference polypeptide or a reference polynucleotide by one or more modifications for example, substitutions, insertions, or deletions. The term “mutation” as used herein is intended to mean one or more intentional substitutions which are made to a polypeptide or polynucleotide.

“Treat,” “treatment,” and like terms refer to both therapeutic treatment and prophylactic or preventative measures, and includes reducing the severity and/or frequency of symptoms, eliminating symptoms and/or the underlying cause of the symptoms, reducing the frequency or likelihood of symptoms and/or their underlying cause, and improving or remediating damage caused, directly or indirectly, by the disease or disorder. Treatment also includes prolonging survival as compared to the expected survival of a subject not receiving treatment. Subjects to be treated include those

that have the disease or disorder as well as those prone to have the disease or disorder or those in which the disease or disorder is to be prevented.

As used herein, “administering to the subject” and similar terms indicate a procedure by which the disclosed modified hIL-2 proteins, immunoconjugates, or pharmaceutical compositions are injected into a subject such that target cells, tissues, or segments of the body of the subject are contacted with the disclosed modified hIL-2 proteins or immunoconjugates comprising the same.

The phrase “therapeutically effective amount” refers to an amount of the modified hIL-2 proteins, immunoconjugates, or pharmaceutical compositions, as described herein, effective to achieve a particular biological or therapeutic result such as, but not limited to, biological or therapeutic results disclosed, described, or exemplified herein. The therapeutically effective amount may vary according to factors such as the disease state, age, sex, and weight of the individual, and the ability of the modified hIL-2 proteins, immunoconjugates, or pharmaceutical compositions to cause a desired response in a subject. Exemplary indicators of a therapeutically effect amount include, for example, improved well-being of the patient, reduction of a disease symptom, arrested or slowed progression of disease symptoms, and/or absence of disease symptoms.

The term “subject” as used herein is intended to mean any animal, in particular, mammals. Thus, the methods are applicable to human and nonhuman animals, although most preferably used with humans. “Subject” and “patient” are used interchangeably herein.

Immunoconjugate and fusion protein are used interchangeably herein.

Modified Human Interleukin-2 (hIL-2) Proteins

Disclosed herein are modified hIL-2 proteins comprising a substitution at amino acid position 20 and a substitution at amino acid position 38 relative to the non-modified hIL-2 amino acid sequence of SEQ ID NO: 345, wherein the modified hIL-2 protein exhibits reduced potency on both a high affinity hIL-2 receptor and on an intermediate affinity hIL-2 receptor relative to a non-modified hIL-2. The disclosed modified hIL-2 proteins are also referred to as “attenuated” hIL-2 herein.

Suitable substitutions at amino acid position 20 include, for example, any one of a D20A, D20S, D20Q, D20M, D20I, D20V, D20N, D20G, D20T, or D20E substitution.

Suitable substitutions at amino acid position 38 include, for example, any one of an R38E, R38N, R38G, R38H, R38I, R38L, R38M, R38F, R38P, R38S, R38T, R38W, R38Y, R38V, R38A, R38Q, R38D, or an R38K substitution.

In some embodiments, any one of the D20A, D20S, D20Q, D20M, D20I, D20V, D20N, D20G, D20T, or D20E substitutions can be combined with an R38E substitution.

The modified hIL-2 proteins can comprise the amino acid sequence of any one of SEQ ID NOs: 134-150, 307, 344, 607-611, 614, 617, or 620. The modified hIL-2 proteins can comprise the amino acid sequence of any one of SEQ ID NOs: 134-150, 307, 344, 608, 611, 614, or 620. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 134. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 135. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 136. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 137. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 138. In some embodiments, the modified hIL-2 proteins comprise

the amino acid sequence of SEQ ID NO: 139. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 140. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 141. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 142. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 143. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 144. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 145. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 146. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 147. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 148. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 149. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 150. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 307. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 344. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 607. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 608. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 609. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 610. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 611. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 614. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 617. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 620. The modified hIL-2 protein of any one of amino acid sequences SEQ ID NOs: 134-150, 307, 344, 607-611, 614, 617, or 620 can further comprise a T3A substitution and/or a C125A substitution. In some embodiments, the modified hIL-2 protein of any one of amino acid sequences SEQ ID NOs: 134-150, 307, 344, 607-611, 614, 617, or 620 further comprises a T3A substitution. In some embodiments, the modified hIL-2 protein of any one of amino acid sequences SEQ ID NOs: 134-150, 307, 344, 607-611, 614, 617, or 620 further comprises a C125A substitution. In some embodiments, the modified hIL-2 protein of any one of amino acid sequences SEQ ID NOs: 134-150, 307, 344, 607-611, 614, 617, or 620 further comprises a T3A substitution and a C125A substitution.

The modified hIL-2 proteins may comprise a D20A substitution and a R38E substitution.

As described herein the term “reduced potency” and related terms such as “reduction in potency” or “attenuation” of IL-2 activity refer to a reduction in potency of the modified hIL-2 as determined by an increased EC_{50} value relative to the EC_{50} value for a non-modified-hIL-2 in an IL-2-dependent assay. As described herein the reduction in potency of the modified hIL-2 will be on both the high affinity and on the intermediate affinity IL-2 receptors. The IL-2-dependent assay for determining potency may be an engineered human erythroleukemic TF1 (TF1+IL-2RB) or a human natural killer NK-92 cell proliferation assay as described herein. In one embodiment, the IL-2-dependent

assay for determining potency is an engineered human erythroleukemic TF1 (TF1+IL-2RB) cell proliferation assay. In another embodiment, the IL-2-dependent assay for determining potency is a human natural killer NK-92 cell proliferation assay. Other IL-2-dependent assays for determining potency may also be a TF1+IL-2R β or a human natural killer NK-92 pSTAT5 assay as described herein. The non-modified-hIL-2 may be a prokaryote-expressed hIL-2 such as Proleukin® (which has the native human IL-2 amino acid sequence apart from a C125S substitution to remove an unbound cysteine, and which does not bear the normal human carbohydrate expression on residue T3), or the non-modified-hIL-2 may be an hIL-2 with the amino acid sequence of SEQ ID NO: 345 or with the amino acid sequence of SEQ ID NO: 345 with a C125S substitution, which is expressed in a mammalian cell line, such as a CHO or HEK cell line.

The modified hIL-2 proteins can further comprise a substitution at amino acid position 3 relative to the non-modified hIL-2 amino acid sequence of SEQ ID NO: 345. A suitable substitution includes, for example, a T3A. In some embodiments, the modified hIL-2 proteins comprise a T3A substitution, a D20A substitution, and a R38E substitution. In some aspects, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 216.

Alternatively, the modified hIL-2 proteins can further comprise a deletion of amino acid position 3 relative to the non-modified hIL-2 amino acid sequence of SEQ ID NO: 345. In some embodiments, the modified hIL-2 proteins comprise a deletion of amino acids 1-3, a D20A substitution, and a R38E substitution. In some aspects, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 218.

The modified hIL-2 proteins can further comprise a deletion or substitution at amino acid position 125 relative to the non-modified hIL-2 amino acid sequence of SEQ ID NO: 345. The substitution at amino acid position 125 can be C125A. In some embodiments, the modified hIL-2 proteins comprise a D20A substitution, a R38E substitution, and a C125A substitution. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 215. In some embodiments, the modified hIL-2 proteins comprise a T3A substitution, a D20A substitution, a R38E substitution, and a C125A substitution. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 217. In some embodiments, the modified hIL-2 proteins comprise a deletion of amino acids 1-3, a D20A substitution, a R38E substitution, and a C125A substitution. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 219.

The modified hIL-2 proteins can exhibit a reduction in potency of at least about 200-fold, at least about 500-fold, at least about 1,000-fold, at least about 2,000-fold, at least about 5,000-fold, at least about 6,500-fold, or at least about 10,000-fold on the high affinity IL-2 receptor (hIL-2R $\alpha\beta\gamma$) relative to a non-modified hIL-2, for example as quantified by a comparison in EC₅₀ values in an hIL-2-dependent cell proliferation assay described herein. In some embodiments, the modified hIL-2 proteins can exhibit a reduction in potency of greater than about 10,000-fold on the high affinity IL-2 receptor (hIL-2R $\alpha\beta\gamma$) relative to a non-modified hIL-2. A greater reduction in hIL-2 potency on the high affinity hIL-2 receptor may be possible and acceptable for the modified hIL-2 proteins described herein, but such a

reduction may not be quantifiable with the methods described herein due to limits of the cell proliferation assay conditions.

In addition, the modified hIL-2 proteins can exhibit a reduction in potency of at least about 200-fold, at least about 500-fold, at least about 1,000-fold, at least about 2,000-fold, at least about 5,000-fold, at least about 6,500-fold, or at least about 10,000-fold on the intermediate affinity IL-2 receptor (hIL-2R $\beta\gamma$) relative to a non-modified hIL-2, for example as quantified by a comparison in EC₅₀ values in an hIL-2-dependent cell proliferation assay described herein. In some embodiments, the modified hIL-2 proteins can exhibit a reduction in potency of greater than about 10,000-fold on the intermediate affinity IL-2 receptor (hIL-2R $\beta\gamma$) relative to a non-modified hIL-2.

The modified hIL-2 proteins can exhibit a reduction in potency of up to about 10,000-fold on the high affinity IL-2 receptor (hIL-2R $\alpha\beta\gamma$) and a reduction in potency of up to about 10,000-fold on the intermediate affinity IL-2 receptor (hIL-2R $\beta\gamma$) relative to a non-modified hIL-2, for example as quantified by a comparison in EC₅₀ values in an hIL-2-dependent cell proliferation assay described herein. The modified hIL-2 proteins can exhibit a reduction in potency of greater than about 10,000-fold on the high affinity IL-2 receptor (hIL-2R $\alpha\beta\gamma$) and a reduction in potency of greater than about 10,000-fold on the intermediate affinity IL-2 receptor (hIL-2R $\beta\gamma$) relative to a non-modified hIL-2.

As demonstrated herein, the modified hIL-2 proteins can be fused to an anti-PD-1 antibody or an antigen-binding fragment thereof. The hIL-2 proteins can be fused to the anti-PD-1 antibody or an antigen-binding fragment thereof at the N-terminus of an antibody light chain, the C-terminus of an antibody light chain, the N-terminus of an antibody heavy chain, the C-terminus of an antibody heavy chain, the N-terminus of the antigen-binding fragment, or the C-terminus of the antigen-binding fragment. In some embodiments, the modified hIL-2 protein is directly fused by a peptide bond to the anti-PD-1 antibody or an antigen-binding fragment thereof. The modified hIL-2 proteins can be, for example, directly fused by a peptide bond to the C-terminal amino acid residue of the anti-PD-1 antibody heavy chain. In some embodiments, the modified hIL-2 protein is fused to the anti-PD-1 antibody or an antigen-binding fragment thereof through a linker.

Fusion of the modified hIL-2 proteins to the antibody or antigen-binding fragments thereof can rescue the modified hIL-2 proteins' ability to bind to and activate the human intermediate affinity IL-2 receptor on PD-1-expressing cells such as T cells and in particular tumor-infiltrating lymphocytes. In some embodiments, the hIL-2 protein that is fused to the antibody or an antigen-binding fragment thereof exhibits potency on the intermediate affinity IL-2 receptor on PD-1-expressing cells that is comparable to the potency of wild type hIL-2 on the intermediate affinity IL-2 receptor.

Fusion of the modified hIL-2 protein to an antibody or antigen-binding fragment thereof can be used to selectively deliver IL-2 signaling to cells expressing the PD-1 target of the antibody or antigen-binding fragment thereof. Without being bound by theory, it is believed that targeting the modified hIL-2 protein to specific cell populations can dramatically amplify the therapeutic effects of the IL-2 (e.g., anti-tumor immunity) without off-target systemic toxicities.

Also disclosed herein are modified human interleukin-2 (hIL-2) proteins comprising a D20A, D20S, D20Q, D20M, D20I, D20V, D20N, D20G, D20T, or D20E substitution at amino acid position 20 and a R38E substitution at amino

acid position 38 relative to the non-modified hIL-2 amino acid sequence of SEQ ID NO: 345.

The modified hIL-2 proteins can comprise the amino acid sequence of any one of SEQ ID NOs: 307, 607-611, 614, 617, or 620. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 307. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 607. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 608. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 609. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 610. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 611. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 614. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 617. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 620. The modified hIL-2 protein of any one of amino acid sequences SEQ ID NOs: 307, 607-611, 614, 617, or 620 can further comprise a T3A substitution and/or a C125A substitution. In some embodiments, the modified hIL-2 protein of any one of amino acid sequences SEQ ID NOs: 307, 607-611, 614, 617, or 620 further comprises a T3A substitution. In some embodiments, the modified hIL-2 protein of any one of amino acid sequences SEQ ID NOs: 307, 607-611, 614, 617, or 620 further comprises a C125A substitution. In some

embodiments, the modified hIL-2 proteins may comprise a D20A substitution and a R38E substitution. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 149.

The modified hIL-2 proteins can further comprise a substitution at amino acid position 3 relative to the non-modified hIL-2 amino acid sequence of SEQ ID NO: 345. A suitable substitution includes, for example, a T3A. In some embodiments, the modified hIL-2 proteins comprise a T3A substitution, a D20A substitution, and a R38E substitution. In some aspects, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 216.

Alternatively, the modified hIL-2 proteins can further comprise a deletion of amino acid position 3 relative to the non-modified hIL-2 amino acid sequence of SEQ ID NO: 345. In some embodiments, the modified hIL-2 proteins comprise a deletion of amino acids 1-3, a D20A substitution, and a R38E substitution. In some aspects, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 218.

The modified hIL-2 proteins can further comprise a deletion or substitution at amino acid position 125 relative to the non-modified hIL-2 amino acid sequence of SEQ ID NO: 345. The substitution at amino acid position 125 can be C125A. In some embodiments, the modified hIL-2 proteins comprise a D20A substitution, a R38E substitution, and a C125A substitution. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 215. In some embodiments, the modified hIL-2 proteins comprise a T3A substitution, a D20A substitution, a R38E substitution, and a C125A substitution. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 217. In some embodiments, the

modified hIL-2 proteins comprise a deletion of amino acids 1-3, a D20A substitution, a R38E substitution, and a C125A substitution. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 219.

The modified hIL-2 proteins can exhibit a reduction in potency of at least about 200-fold, at least about 500-fold, at least about 1,000-fold, at least about 2,000-fold, at least about 5,000-fold, at least about 6,500-fold, or at least about 10,000-fold on the high affinity IL-2 receptor (hIL-2R $\alpha\beta\gamma$) relative to a non-modified hIL-2, for example as quantified by a comparison in EC_{50} values in an hIL-2-dependent cell proliferation assay described herein. In some embodiments, the modified hIL-2 proteins can exhibit a reduction in potency of greater than about 10,000-fold on the high affinity IL-2 receptor (hIL-2R $\alpha\beta\gamma$) relative to a non-modified hIL-2. A greater reduction in hIL-2 potency on the high affinity hIL-2 receptor may be possible and acceptable for the modified hIL-2 proteins described herein, but such a reduction may not be quantifiable with the methods described herein due to limits of the cell proliferation assay conditions.

In addition, the modified hIL-2 proteins can exhibit a reduction in potency of at least about 200-fold, at least about 500-fold, at least about 1,000-fold, at least about 2,000-fold, at least about 5,000-fold, at least about 6,500-fold, or at least about 10,000-fold on the intermediate affinity IL-2 receptor (hIL-2R $\beta\gamma$) relative to a non-modified hIL-2, for example as quantified by a comparison in EC_{50} values in an hIL-2-dependent cell proliferation assay described herein. In some embodiments, the modified hIL-2 proteins can exhibit a reduction in potency of greater than about 10,000-fold on the intermediate affinity IL-2 receptor (hIL-2R $\beta\gamma$) relative to a non-modified hIL-2.

The modified hIL-2 proteins can exhibit a reduction in potency of up to about 10,000-fold on the high affinity IL-2 receptor (hIL-2R $\beta\gamma$) and a reduction in potency of up to about 10,000-fold on the intermediate affinity IL-2 receptor (hIL-2R $\beta\gamma$) relative to a non-modified hIL-2, for example as quantified by a comparison in EC_{50} values in an hIL-2-dependent cell proliferation assay described herein. The modified hIL-2 proteins can exhibit a reduction in potency of greater than about 10,000-fold on the high affinity IL-2 receptor (hIL-2R $\alpha\beta\gamma$) and a reduction in potency of greater than about 10,000-fold on the intermediate affinity IL-2 receptor (hIL-2R $\beta\gamma$) relative to a non-modified hIL-2.

As demonstrated herein, the modified hIL-2 proteins can be fused to an anti-PD-1 antibody or an antigen-binding fragment thereof. The hIL-2 proteins can be fused to the anti-PD-1 antibody or an antigen-binding fragment thereof at the N-terminus of an antibody light chain, the C-terminus of an antibody light chain, the N-terminus of an antibody heavy chain, the C-terminus of an antibody heavy chain, the N-terminus of the antigen-binding fragment, or the C-terminus of the antigen-binding fragment. In some embodiments, the modified hIL-2 protein is directly fused by a peptide bond to the anti-PD-1 antibody or an antigen-binding fragment thereof. The modified hIL-2 proteins can be, for example, directly fused by a peptide bond to the C-terminal amino acid residue of the anti-PD-1 antibody heavy chain. In some embodiments, the modified hIL-2 protein is fused to the anti-PD-1 antibody or an antigen-binding fragment thereof through a linker.

Fusion of the modified hIL-2 proteins to the antibody or antigen-binding fragments thereof can rescue the modified hIL-2 proteins' ability to bind to and activate the human intermediate affinity IL-2 receptor on PD-1-expressing cells

such as T cells and in particular tumor-infiltrating lymphocytes. In some embodiments, the hIL-2 protein that is fused to the antibody or an antigen-binding fragment thereof exhibits potency on the intermediate affinity IL-2 receptor on PD-1-expressing cells that is comparable to the potency of wild type hIL-2 on the intermediate affinity IL-2 receptor.

Fusion of the modified hIL-2 protein to an antibody or antigen-binding fragment thereof can be used to selectively deliver IL-2 signaling to cells expressing the PD-1 target of the antibody or antigen-binding fragment thereof. Without being bound by theory, it is believed that targeting the modified hIL-2 protein to specific cell populations can dramatically amplify the therapeutic effects of the IL-2 (e.g., anti-tumor immunity) without off-target systemic toxicities. Human Anti-Human Programmed Cell Death Protein-1 (hPD-1) Antibodies

Disclosed herein are human antibody molecules, or antigen-binding fragments thereof, that immunospecifically bind to hPD-1, wherein the human antibody molecule or antigen-binding fragment thereof comprises:

- a) a heavy chain complementarity determining region 1 (CDR1) comprising the amino acid sequence of SEQ ID NO: 418, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 419, a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 420, a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 421, a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 422, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 423;
- b) a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 386, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 387, a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 388, a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 389, a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 390, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 391;
- c) a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 396, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 397, a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 398, a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 399, a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 400, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 401; or
- d) a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 406, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 407, a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 408, a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 409, a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 410, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 411.

In some embodiments, the human antibody molecules, or antigen-binding fragments thereof, comprise a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 418, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 419, a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 420, a light chain CDR1 comprising the amino acid sequence of SEQ ID

NO: 421, a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 422, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 423 (referred to herein as "H7-632").

In some embodiments, the human antibody molecules, or antigen-binding fragments thereof, comprise a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 386, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 387, a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 388, a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 389, a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 390, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 391 (referred to herein as "2H7").

In some embodiments, the human antibody molecules, or antigen-binding fragments thereof, comprise a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 396, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 397, a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 398, a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 399, a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 400, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 401 (referred to herein as "C51E6-5").

In some embodiments, the human antibody molecules, or antigen-binding fragments thereof, comprise a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 406, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 407, a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 408, a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 409, a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 410, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 411 (referred to herein as "A2").

The disclosed human antibody molecules or antigen-binding fragments thereof, can exhibit one or more of the following activities:

- Bind to PD-1 without inhibiting PD-L1 binding to PD-1;
- Bind to PD-1 in the presence of standard-of-care anti-PD-1 antibodies used in the clinic (e.g., KEYTRUDAX and OPDIVOX);
- Be highly selective for PD-1 and do not immunospecifically bind other related B7 family members; and
- Bind to PD-1 on activated human T cells (EC_{50} ~0.1-0.2 nM in a flow cytometry binding assay).

The human antibody molecules, or antigen-binding fragments thereof, can comprise a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 416 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 417 (referred to herein as "H7-632").

The human antibody molecules, or antigen-binding fragments thereof, can comprise a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 384 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 385 (referred to herein as "2H7").

The human antibody molecules, or antigen-binding fragments thereof, can comprise a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 394 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 395 (referred to herein as "C51E6-5").

The human antibody molecules, or antigen-binding fragments thereof, can comprise a heavy chain variable region

comprising the amino acid sequence of SEQ ID NO: 404 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 405 (referred to herein as "A2").

The human antibody molecules, or antigen-binding fragments thereof, can comprise a human IgG1 heavy chain constant region.

The human antibody molecules, or antigen binding fragments thereof, can have substitutions or deletions within the constant region to minimize Fc-mediated immune effector function, such as FcγRIIIA-mediated antibody-dependent cell-mediated cytotoxicity (ADCC), FcγRI- and FcγRIIa-dependent antibody-dependent cellular phagocytosis (ADCP), and C1q binding-mediated complement-dependent cytotoxicity (CDC). In some embodiments, the human antibody molecules comprise a L235A substitution, wherein the amino acid numbering is according to EU numbering. In some embodiments, the human antibody molecules comprise a G237A substitution, wherein the amino acid numbering is according to EU numbering. In some embodiments, the human antibody molecules comprise an L235A and a G237A substitution, wherein the amino acid numbering is according to EU numbering.

The human antibody molecules, or antigen-binding fragments thereof, can comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 414 and a light chain comprising the amino acid sequence of SEQ ID NO: 415 (referred to herein as "H7-632-hIgG1-LAGA").

The human antibody molecules, or antigen-binding fragments thereof, can comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 424 and a light chain comprising the amino acid sequence of SEQ ID NO: 425 (referred to herein as "2H7-hIgG4").

The human antibody molecules, or antigen-binding fragments thereof, can comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 426 and a light chain comprising the amino acid sequence of SEQ ID NO: 427 (referred to herein as "C51E6-5-hIgG4").

The human antibody molecules, or antigen-binding fragments thereof, can comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 428 and a light chain comprising the amino acid sequence of SEQ ID NO: 429 (referred to herein as "A2-hIgG4").

The human antibody molecules, or antigen-binding fragments thereof, can be fused to a modified hIL-2 protein comprising a substitution at amino acid position 20 and a substitution at amino acid position 38 relative to the non-modified hIL-2 amino acid sequence of SEQ ID NO: 345. The human antibody molecule, or antigen-binding fragments thereof, can be fused to any of the herein disclosed modified hIL-2 proteins.

When not fused to the antibody molecule or antigen-binding fragment thereof, the modified hIL-2 protein can exhibit reduced potency on both a high affinity hIL-2 receptor and on an intermediate affinity hIL-2 receptor relative to a non-modified hIL-2.

Suitable substitutions at amino acid position 20 of the modified hIL-2 include, for example, any one of a D20A, D20S, D20Q, D20M, D20I, D20V, D20N, D20G, D20T, or D20E substitution.

Suitable substitutions at amino acid position 38 of the modified hIL-2 protein include, for example, any one of an R38E, R38N, R38G, R38H, R38I, R38L, R38M, R38F, R38P, R38S, R38T, R38W, R38Y, R38V, R38A, R38Q, R38D, or a R38K substitution.

In some embodiments, any one of the D20A, D20S, D20Q, D20M, D20I, D20V, D20N, D20G, D20T, or D20E substitutions can be combined with an R38E substitution.

The modified hIL-2 proteins can comprise the amino acid sequence of any one of SEQ ID NOs: 134-150, 307, 344, 607-611, 614, 617, or 620. The modified hIL-2 proteins can comprise the amino acid sequence of any one of SEQ ID NOs: 134-150, 307, 344, 608, 611, 614, or 620. In some embodiments, the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 134. In some embodiments, the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 135. In some embodiments, the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 136. In some embodiments, the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 137. In some embodiments, the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 138. In some embodiments, the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 139. In some embodiments, the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 140. In some embodiments, the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 141. In some embodiments, the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 142. In some embodiments, the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 143. In some embodiments, the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 144. In some embodiments, the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 145. In some embodiments, the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 146. In some embodiments, the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 147. In some embodiments, the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 148. In some embodiments, the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 149. In some embodiments, the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 150. In some embodiments, the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 307. In some embodiments, the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 344. In some embodiments, the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 607. In some embodiments, the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 608. In some embodiments, the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 609. In some embodiments, the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 610. In some embodiments, the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 611. In some embodiments, the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 614. In some embodiments, the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 617. In some embodiments, the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 620. The modified hIL-2 protein of any one of amino acid sequences SEQ ID NOs: 134-150, 307, 344, 607-611, 614, 617, or 620 can further comprise a T3A substitution and/or a C125A substitution. In some embodiments, the modified hIL-2 protein of any one of amino acid sequences SEQ ID NOs: 134-150, 307, 344, 607-611, 614, 617, or 620 further comprises a T3A substitution. In some embodiments, the modified hIL-2 protein of any one of amino acid sequences SEQ ID NOs: 134-150, 307, 344, 607-611, 614, 617, or 620 further comprises a C125A substitution. In some embodiments, the modified hIL-2 protein of any one of amino acid sequences SEQ ID NOs:

134-150, 307, 344, 607-611, 614, 617, or 620 further comprises a T3A substitution and a C125A substitution.

The modified hIL-2 protein can comprise a D20A substitution and a R38E substitution.

The modified hIL-2 protein can further comprise a substitution at amino acid position 3 relative to the non-modified hIL-2 amino acid sequence of SEQ ID NO: 345. A suitable substitution includes, for example, a T3A. In some embodiments, the modified hIL-2 protein comprises a T3A substitution, a D20A substitution, and a R38E substitution. In some aspects, the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 216.

Alternatively, the modified hIL-2 protein can further comprise a deletion of amino acid position 3 relative to the non-modified hIL-2 amino acid sequence of SEQ ID NO: 345. In some embodiments, the modified hIL-2 protein comprises a deletion of amino acids 1-3, a D20A substitution, and a R38E substitution. In some aspects, the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 218.

The modified hIL-2 protein can further comprise a deletion or substitution at amino acid position 125 relative to the non-modified hIL-2 amino acid sequence of SEQ ID NO: 345. The substitution at amino acid position 125 can be C125A. In some embodiments, the modified hIL-2 protein comprises a D20A substitution, a R38E substitution, and a C125A substitution. In some embodiments, the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 215. In some embodiments, the modified hIL-2 protein comprises a T3A substitution, a D20A substitution, a R38E substitution, and a C125A substitution. In some embodiments, the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 217. In some embodiments, the modified hIL-2 protein comprises a deletion of amino acids 1-3, a D20A substitution, a R38E substitution, and a C125A substitution. In some embodiments, the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 219.

When not fused to the human antibody molecules or antigen-binding fragments thereof, the modified hIL-2 proteins can exhibit a reduction in potency of at least about 200-fold, at least about 500-fold, at least about 1,000-fold, at least about 2,000-fold, at least about 5,000-fold, at least about 6,500-fold, or at least about 10,000-fold on the high affinity IL-2 receptor (hIL-2R $\alpha\beta\gamma$) relative to a non-modified hIL-2, for example as quantified by a comparison in EC₅₀ values in an hIL-2-dependent cell proliferation assay described herein. In some embodiments, when not fused to the human antibody molecules or antigen-binding fragments thereof, the modified hIL-2 proteins can exhibit a reduction in potency of greater than about 10,000-fold on the high affinity IL-2 receptor (hIL-2R $\alpha\beta\gamma$) relative to a non-modified hIL-2. A greater reduction in hIL-2 potency on the high affinity hIL-2 receptor may be possible and acceptable for the modified hIL-2 proteins described herein, but such a reduction may not be quantifiable with the methods described herein due to limits of the cell proliferation assay conditions.

In addition, when not fused to the human antibody molecules or antigen-binding fragments thereof, the modified hIL-2 proteins can exhibit a reduction in potency of at least about 200-fold, at least about 500-fold, at least about 1,000-fold, at least about 2,000-fold, at least about 5,000-fold, at least about 6,500-fold, or at least about 10,000-fold on the intermediate affinity IL-2 receptor (hIL-2R $\beta\gamma$) relative to a non-modified hIL-2, for example as quantified by a comparison in EC₅₀ values in an hIL-2-dependent cell proliferation

assay described herein. In some embodiments, when not fused to the human antibody molecules or antigen-binding fragments thereof, the modified hIL-2 proteins can exhibit a reduction in potency of greater than about 10,000-fold on the intermediate affinity IL-2 receptor (hIL-2R $\beta\gamma$) relative to a non-modified hIL-2.

When not fused to the human antibody molecules or antigen-binding fragments thereof, the modified hIL-2 proteins can exhibit a reduction in potency of up to about 10,000-fold on the high affinity IL-2 receptor (hIL-2R $\alpha\beta\gamma$) and a reduction in potency of up to about 10,000-fold on the intermediate affinity IL-2 receptor (hIL-2R $\beta\gamma$) relative to a non-modified hIL-2, for example as quantified by a comparison in EC₅₀ values in an hIL-2-dependent cell proliferation assay described herein. When not fused to the human antibody molecules or antigen-binding fragments thereof, the modified hIL-2 proteins can exhibit a reduction in potency of greater than about 10,000-fold on the high affinity IL-2 receptor (hIL-2R $\alpha\beta\gamma$) and a reduction in potency of greater than about 10,000-fold on the intermediate affinity IL-2 receptor (hIL-2R $\beta\gamma$) relative to a non-modified hIL-2.

Fusion of the modified hIL-2 proteins to the antibody or antigen-binding fragments thereof can rescue the modified hIL-2 proteins' ability to bind to and activate the human intermediate affinity IL-2 receptor on PD-1-expressing cells such as T cells and in particular tumor-infiltrating lymphocytes. In some embodiments, the hIL-2 protein that is fused to the antibody or an antigen-binding fragment thereof exhibits potency on the intermediate affinity IL-2 receptor on PD-1-expressing cells that is comparable to the potency of wild type hIL-2 on the intermediate affinity IL-2 receptor.

The modified hIL-2 proteins can be fused to the human antibody molecules or antigen-binding fragments thereof at the N-terminus of an antibody light chain, the C-terminus of an antibody light chain, the N-terminus of an antibody heavy chain, the C-terminus of an antibody heavy chain, the N-terminus of the antigen-binding fragment, or the C-terminus of the antigen-binding fragment. In some embodiments, the hIL-2 protein is directly fused by a peptide bond to the antibody or an antigen-binding fragment thereof. The hIL-2 can be, for example, directly fused by a peptide bond to the C-terminal amino acid residue of the antibody heavy chain. In some embodiments, the hIL-2 protein is fused to the antibody or an antigen-binding fragment thereof through a linker.

Fusion of the human antibody molecules or antigen-binding fragments thereof to the modified hIL-2 proteins can be used to selectively deliver IL-2 signaling to cells expressing PD-1. Without being bound by theory, it is believed that targeting the modified hIL-2 protein to specific cell populations expressing PD-1 can dramatically amplify the therapeutic effects of the IL-2 (e.g., anti-tumor immunity) while reducing or minimizing off-target systemic toxicities.

Immunoconjugates

Disclosed herein are immunoconjugates comprising any of the herein disclosed modified hIL-2 proteins and any of the herein disclosed human antibody molecules, or antigen-binding fragments thereof. The immunoconjugates can comprise:

- a modified hIL-2 protein comprising a substitution at amino acid position 20 and a substitution at amino acid position 38 relative to the non-modified hIL-2 amino acid sequence of SEQ ID NO: 345; and
- a human antibody molecule, or antigen-binding fragment thereof, that immunospecifically binds to hPD-1,

wherein the human antibody molecule or antigen-binding fragment thereof comprises:

- (i) a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 418, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 419, a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 420, a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 421, a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 422, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 423;
- (ii) a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 386, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 387, a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 388, a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 389, a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 390, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 391;
- (iii) a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 396, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 397, a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 398, a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 399, a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 400, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 401; or
- (iv) a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 406, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 407, a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 408, a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 409, a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 410, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 411.

Suitable substitutions at amino acid position 20 of the modified hIL-2 portion of the immunoconjugates include, for example, any of a D20A, D20S, D20Q, D20M, D20I, D20V, D20N, D20G, D20T, or D20E substitution.

Suitable substitutions at amino acid position 38 of the modified hIL-2 portion of the immunoconjugates include, for example, any of an R38E, R38N, R38G, R38H, R38I, R38L, R38M, R38F, R38P, R38S, R38T, R38W, R38Y, R38V, R38A, R38Q, R38D, or a R38K substitution.

In some embodiments, any one of the D20A, D20S, D20Q, D20M, D20I, D20V, D20N, D20G, D20T, or D20E substitutions can be combined with an R38E substitution.

The modified hIL-2 protein portion of the immunoconjugates can comprise the amino acid sequence of any one of SEQ ID NOs: 134-150, 307, 344, 607-611, 614, 617, or 620. The modified hIL-2 protein portion of the immunoconjugates can comprise the amino acid sequence of any one of SEQ ID NOs: 134-150, 307, 344, 608, 611, 614, or 620. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 134. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 135. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence

of SEQ ID NO: 137. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 138. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 139. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 140. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 141. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 142. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 143. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 144. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 145. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 146. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 147. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 148. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 149. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 150. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 307. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 344. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 607. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 608. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 609. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 610. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 611. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 614. In some embodiments, the modified hIL-2 proteins comprise the amino acid sequence of SEQ ID NO: 617. In some embodiments, the modified hIL-2 protein of any one of amino acid sequences SEQ ID NOs: 134-150, 307, 344, 607-611, 614, 617, or 620 can further comprise a T3A substitution and/or a C125A substitution. In some embodiments, the modified hIL-2 protein of any one of amino acid sequences SEQ ID NOs: 134-150, 307, 344, 607-611, 614, 617, or 620 further comprises a T3A substitution. In some embodiments, the modified hIL-2 protein of any one of amino acid sequences SEQ ID NOs: 134-150, 307, 344, 607-611, 614, 617, or 620 further comprises a C125A substitution. In some embodiments, the modified hIL-2 protein of any one of amino acid sequences SEQ ID NOs: 134-150, 307, 344, 607-611, 614, 617, or 620 further comprises a T3A substitution and a C125A substitution.

The modified hIL-2 protein portion of the immunoconjugates can comprise a D20A substitution and a R38E substitution.

The modified hIL-2 protein portion of the immunoconjugates can further comprise a substitution at amino acid position 3 relative to the non-modified hIL-2 amino acid sequence of SEQ ID NO: 345. A suitable substitution includes, for example, a T3A. In some embodiments, the modified hIL-2 protein portion of the immunoconjugates comprise a T3A substitution, a D20A substitution, and a R38E substitution. In some aspects, the modified hIL-2

protein portion of the immunoconjugates comprise the amino acid sequence of SEQ ID NO: 216.

Alternatively, the modified hIL-2 protein portion of the immunoconjugates can further comprise a deletion of amino acid position 3 relative to the non-modified hIL-2 amino acid sequence of SEQ ID NO: 345. In some embodiments, the modified hIL-2 protein portion of the immunoconjugates comprise a deletion of amino acids 1-3, a D20A substitution, and a R38E substitution. In some aspects, the modified hIL-2 protein portion of the immunoconjugates comprise the amino acid sequence of SEQ ID NO: 218.

The modified hIL-2 protein portion of the immunoconjugates can further comprise a deletion or substitution at amino acid position 125 relative to the non-modified hIL-2 amino acid sequence of SEQ ID NO: 345. The substitution at amino acid position 125 can be C125A. In some embodiments, the modified hIL-2 protein portion of the immunoconjugates comprise a D20A substitution, a R38E substitution, and a C125A substitution. In some embodiments, the modified hIL-2 protein portion of the immunoconjugates comprise the amino acid sequence of SEQ ID NO: 215. In some embodiments, the modified hIL-2 protein portion of the immunoconjugates comprise a T3A substitution, a D20A substitution, a R38E substitution, and a C125A substitution. In some embodiments, the modified hIL-2 protein portion of the immunoconjugates comprise the amino acid sequence of SEQ ID NO: 217. In some embodiments, the modified hIL-2 protein portion of the immunoconjugates comprise a deletion of amino acids 1-3, a D20A substitution, a R38E substitution, and a C125A substitution. In some embodiments, the modified hIL-2 protein portion of the immunoconjugates comprise the amino acid sequence of SEQ ID NO: 219.

The modified hIL-2 protein portion of the immunoconjugates can exhibit a reduction in potency of at least about 200-fold, at least about 500-fold, at least about 1,000-fold, at least about 2,000-fold, at least about 5,000-fold, at least about 6,500-fold, or at least about 10,000-fold on the high affinity IL-2 receptor (hIL-2R $\alpha\beta\gamma$) relative to a non-modified hIL-2, for example as quantified by a comparison in EC₅₀ values in an hIL-2-dependent cell proliferation assay described herein. In some embodiments, the modified hIL-2 protein portion of the immunoconjugates can exhibit a reduction in potency of greater than about 10,000-fold on the high affinity IL-2 receptor (hIL-2R $\alpha\beta\gamma$) relative to a non-modified hIL-2. A greater reduction in hIL-2 potency on the high affinity hIL-2 receptor may be possible and acceptable for the modified hIL-2 proteins described herein, but such a reduction may not be quantifiable with the methods described herein due to limits of the cell proliferation assay conditions.

In addition, the modified hIL-2 protein portion of the immunoconjugates can exhibit a reduction in potency of at least about 200-fold, at least about 500-fold, at least about 1,000-fold, at least about 2,000-fold, at least about 5,000-fold, at least about 6,500-fold, or at least about 10,000-fold on the intermediate affinity IL-2 receptor (hIL-2R $\beta\gamma$) relative to a non-modified hIL-2, for example as quantified by a comparison in EC₅₀ values in an hIL-2-dependent cell proliferation assay described herein. In some embodiments, the modified hIL-2 protein portion of the immunoconjugates can exhibit a reduction in potency of greater than about 10,000-fold on the intermediate affinity IL-2 receptor (hIL-2R $\beta\gamma$) relative to a non-modified hIL-2.

The modified hIL-2 protein portion of the immunoconjugates can exhibit a reduction in potency of up to about 10,000-fold on the high affinity IL-2 receptor (hIL-2R $\alpha\beta\gamma$)

and a reduction in potency of up to about 10,000-fold on the intermediate affinity IL-2 receptor (hIL-2R $\beta\gamma$) relative to a non-modified hIL-2, for example as quantified by a comparison in EC₅₀ values in an hIL-2-dependent cell proliferation assay described herein. The modified hIL-2 protein portion of the immunoconjugates can exhibit a reduction in potency of greater than about 10,000-fold on the high affinity IL-2 receptor (hIL-2R $\alpha\beta\gamma$) and a reduction in potency of greater than about 10,000-fold on the intermediate affinity IL-2 receptor (hIL-2R $\beta\gamma$) relative to a non-modified hIL-2.

The hIL-2 protein portion of the immunoconjugates can be fused to the antibody or an antigen-binding fragment thereof at the N-terminus of an antibody light chain, the C-terminus of an antibody light chain, the N-terminus of an antibody heavy chain, the C-terminus of an antibody heavy chain, the N-terminus of the antigen-binding fragment, or the C-terminus of the antigen-binding fragment. In some embodiments, the hIL-2 protein portion of the immunoconjugates is directly fused by a peptide bond to the human antibody molecule or an antigen-binding fragment thereof. The hIL-2 protein portion of the immunoconjugates can be, for example, directly fused by a peptide bond to the C-terminal amino acid residue of the antibody heavy chain. In some embodiments, the hIL-2 protein portion of the immunoconjugates is fused to the human antibody molecule or an antigen-binding fragment thereof through a linker.

Fusion of the modified hIL-2 proteins to the human antibody molecules or antigen-binding fragments thereof can rescue the modified hIL-2 proteins' ability to activate the intermediate affinity IL-2 receptor. In some embodiments, the immunoconjugate is able to activate the intermediate affinity IL-2 receptor to a degree that is comparable to wild type hIL-2 activation of the intermediate affinity IL-2 receptor.

In some embodiments, the human antibody molecule, or antigen-binding fragment thereof, portion of the immunoconjugates comprise a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 418, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 419, a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 420, a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 421, a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 422, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 423.

In some embodiments, the human antibody molecule, or antigen-binding fragment thereof, portion of the immunoconjugates comprise a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 386, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 387, a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 388, a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 389, a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 390, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 391.

In some embodiments, the human antibody molecule, or antigen-binding fragment thereof, portion of the immunoconjugates comprise a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 396, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 397, a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 398, a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 399, a light chain CDR2 comprising the amino acid sequence of SEQ ID

NO: 400, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 401.

In some embodiments, the human antibody molecule, or antigen-binding fragment thereof, portion of the immunoconjugates comprise a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 406, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 407, a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 408, a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 409, a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 410, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 411.

The human antibody molecule, or antigen-binding fragment thereof, portion of the immunoconjugates can comprise a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 416 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 417.

The human antibody molecule, or antigen-binding fragment thereof, portion of the immunoconjugates can comprise a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 384 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 385.

The human antibody molecule, or antigen-binding fragment thereof, portion of the immunoconjugates can comprise a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 394 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 395.

The human antibody molecule, or antigen-binding fragment thereof, portion of the immunoconjugates can comprise a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 404 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 405.

The human antibody molecule, or antigen-binding fragment thereof, portion of the immunoconjugates can comprise an IgG1 heavy chain constant region.

The human antibody molecule, or antigen-binding fragment thereof, portion of the immunoconjugates can have substitutions or deletions within the constant region to minimize Fc-mediated immune effector function, such as FcγRIIIA-mediated antibody-dependent cell-mediated cytotoxicity (ADCC), FcγRI- and FcγRIIa-dependent antibody-dependent cellular phagocytosis (ADCP), and C1q binding-mediated complement-dependent cytotoxicity (CDC). In some embodiments, the human antibody molecule portion of the immunoconjugates comprise a L235A substitution, wherein the amino acid numbering is according to EU numbering. In some embodiments, the human antibody molecule portion of the immunoconjugates comprise a G237A substitution, wherein the amino acid numbering is according to EU numbering. In some embodiments, the human antibody molecule portion of the immunoconjugates comprise an L235A and a G237A substitution, wherein the amino acid numbering is according to EU numbering.

The human antibody molecule, or antigen-binding fragment thereof, portion of the immunoconjugates can comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 414 and a light chain comprising the amino acid sequence of SEQ ID NO: 415.

The human antibody molecule, or antigen-binding fragment thereof, portion of the immunoconjugates can comprise a heavy chain comprising the amino acid sequence of

SEQ ID NO: 424 and a light chain comprising the amino acid sequence of SEQ ID NO: 425.

The human antibody molecule, or antigen-binding fragment thereof, portion of the immunoconjugates can comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 426 and a light chain comprising the amino acid sequence of SEQ ID NO: 427.

The human antibody molecule, or antigen-binding fragment thereof, portion of the immunoconjugates can comprise a heavy chain comprising the amino acid sequence of SEQ ID NO: 428 and a light chain comprising the amino acid sequence of SEQ ID NO: 429.

The immunoconjugates can have one or more of the following properties:

Binds to PD-1 but does not inhibit PD-L1 binding to PD-1;

Binds to PD-1 in the presence of standard-of-care anti-PD-1 antibodies used in the clinic (e.g., KEYTRUDA[®] and OPDIVOR[®]);

Is highly selective for PD-1 and does not immunospecifically bind other related B7 family members;

Binds PD-1 on activated human T cells ($EC_{50} \sim 0.1-0.2$ nM in a flow binding assay);

Has reduction in potency of at least about 200-fold, at least about 500-fold, at least about 1,000-fold, at least about 2,000-fold, at least about 5,000-fold, at least about 6,500-fold, or at least about 10,000-fold on the high affinity IL-2 receptor (hIL-2R $\alpha\beta\gamma$) relative to a non-modified hIL-2, for example as quantified by a comparison in EC_{50} values in an hIL-2-dependent cell proliferation assay described herein. In some embodiments, the modified hIL-2 protein portion of the immunoconjugates can exhibit a reduction in potency of greater than about 10,000-fold on the high affinity IL-2 receptor (hIL-2R $\alpha\beta\gamma$) relative to a non-modified hIL-2. A greater reduction in hIL-2 potency on the high affinity hIL-2 receptor may be possible and acceptable for the modified hIL-2 proteins described herein, but such a reduction may not be quantifiable with the methods described herein due to limits of the cell proliferation assay conditions;

Has a reduction in potency of at least about 200-fold, at least about 500-fold, at least about 1,000-fold, at least about 2,000-fold, at least about 5,000-fold, at least about 6,500-fold, or at least about 10,000-fold on the intermediate affinity IL-2 receptor (hIL-2R $\beta\gamma$) relative to a non-modified hIL-2, for example as quantified by a comparison in EC_{50} values in an hIL-2-dependent cell proliferation assay described herein. In some embodiments, the modified hIL-2 protein portion of the immunoconjugates can exhibit a reduction in potency of greater than about 10,000-fold on the intermediate affinity IL-2 receptor (hIL-2R $\beta\gamma$) relative to a non-modified hIL-2;

Rescues and expands PD-1-expressing human memory T cell subsets in a GvHD animal model; and

Has minimal or no impact on body weight, blood chemistry, or hematology parameters after single dose at 1 and 10 mg/kg in cynomolgus monkeys.

In some embodiments, the immunoconjugate comprises a modified hIL-2 protein comprising a T3A substitution, a R38E substitution, a D20A substitution, and a C125A substitution fused to the C-terminus of the antibody heavy chain of a human anti-hPD-1 antibody comprising a human IgG1 framework with a L235A substitution and a G237A substitution. In some embodiments, the immunoconjugate comprises a light chain comprising the amino acid sequence of

SEQ ID NO: 415 and a heavy chain-hIL-2 protein fusion comprising the amino acid sequence of SEQ ID NO: 532.

The disclosed immunoconjugates can selectively deliver IL-2 signaling to PD-1-expressing T cells. The human antibody molecule, or antigen-binding fragment thereof, portion of the immunoconjugate is utilized solely to deliver the modified hIL-2 to PD-1-expressing cells and does not block PD-1 receptor function, as do classical anti-PD-1 inhibitor antibodies such as OPDIVOR and KEYTRUDAR. The primary mechanism-of-action of the herein disclosed immunoconjugates is via the T cell selective activity of IL-2. The human PD-1 receptor is primarily expressed on a minor subset of T cells with potent tumor reactivity. Without being bound by theory, it is believed that targeting the modified hIL-2 protein portion of the immunoconjugate to this population of T cells can dramatically amplify anti-tumor immunity while reducing or minimizing off-target systemic IL-2-mediated toxicities mediated by cell populations that lack PD-1 expression.

Pharmaceutical Compositions, Polynucleotides, Vectors, and Cells

Disclosed herein are pharmaceutical compositions comprising any of the herein disclosed modified hIL-2 proteins, any of the herein disclosed human antibody molecules or antigen-binding fragments thereof, or any of the herein disclosed immunoconjugates. In some embodiments, the pharmaceutical compositions comprise any of the herein disclosed modified hIL-2 proteins. In some embodiments, the pharmaceutical compositions comprise any of the herein disclosed human antibody molecules or antigen-binding fragments thereof. In some embodiments, the pharmaceutical compositions comprise any of the herein disclosed immunoconjugates.

Disclosed herein are polynucleotides comprising a nucleic acid sequence encoding any of the herein disclosed modified hIL-2 proteins, any of the herein disclosed human antibody molecules or antigen-binding fragments thereof, or any of the herein disclosed immunoconjugates. In some embodiments, the polynucleotides comprise a nucleic acid sequence encoding any of the herein disclosed modified hIL-2 proteins. In some embodiments, the polynucleotides comprise a nucleic acid sequence encoding any of the herein disclosed human antibody molecules or antigen-binding fragments thereof. In some embodiments, the polynucleotides comprise a nucleic acid sequence encoding any of the herein disclosed immunoconjugates.

Disclosed herein are vectors comprising a polynucleotide comprising a nucleic acid sequence that encodes any of the herein disclosed modified hIL-2 proteins, any of the herein disclosed human antibody molecules or antigen-binding fragments thereof, or any of the herein disclosed immunoconjugates. In some embodiments, the vectors comprise a polynucleotide comprising a nucleic acid sequence that encodes any of the herein disclosed modified hIL-2 proteins. In some embodiments, the vectors comprise a polynucleotide comprising a nucleic acid sequence that encodes any of the herein disclosed human antibody molecules or antigen-binding fragments thereof. In some embodiments, the vectors comprise a polynucleotide comprising a nucleic acid sequence that encodes any of the herein disclosed immunoconjugates.

Also disclosed herein are transformed cells comprising any of the herein disclosed vectors.

Methods of Treatment and Uses

Disclosed herein are methods of treating a disease or disorder in a subject, the methods comprising administering a therapeutically effective amount of any of the herein

disclosed immunoconjugates or pharmaceutical compositions to the subject to thereby treat the disease.

Also disclosed are uses of any of the herein disclosed immunoconjugates or pharmaceutical compositions in the preparation of a medicament for the treatment of a disease. Also disclosed are uses of any of the herein described immunoconjugates or pharmaceutical compositions for the treatment of a disease or disorder.

The disclosed immunoconjugates and pharmaceutical compositions can be used to treat diseases or disorders in which stimulation of the subject's immune system would be beneficial. In some embodiments, the subject has an insufficient or deficient immune response and the disclosed immunoconjugates and pharmaceutical compositions stimulate the subject's immune response. The antibody portion of the immunoconjugate can serve to direct the modified hIL-2 protein to the subject's immune cells by, for example, binding to an antigen expressed on the surface of the immune cell. In the case of the disclosed modified hIL-2 protein-human anti-hPD-1 antibody immunoconjugates, for example, the anti-PD-1 antibody (or antigen-binding fragment thereof) portion of the immunoconjugate can bind PD-1 expressed on T cells, thereby delivering the modified hIL-2 protein to the T cells. Targeting the modified IL-2 protein to specific cells can dramatically amplify the therapeutic efficacy of the IL-2 protein without off-target systemic toxicities mediated by cell populations that lack the antigen expression. The disclosed methods and uses can be used to treat, for example, cancer, autoimmune diseases and inflammatory diseases, and chronic infections and infectious diseases. Exemplary cancers include bladder cancer, brain cancer, head and neck cancer, pancreatic cancer, lung cancer, non-small cell lung carcinoma, breast cancer, ovarian cancer, uterine cancer, cervical cancer, endometrial cancer, esophageal cancer, colon cancer, colorectal cancer, rectal cancer, gastric cancer, prostate cancer, blood cancer, skin cancer, melanoma, squamous cell carcinoma, bone cancer, and kidney cancer. Exemplary autoimmune diseases and inflammatory disease include systemic lupus erythematosus (SLE), Type 1 diabetes, rheumatoid arthritis, ankylosing spondylitis, psoriasis, Behcet's disease, granulomatosis with polyangiitis, Takayasu's disease, Crohn's disease, ulcerative colitis, autoimmune hepatitis, sclerosing cholangitis, Sjoren's syndrome, alopecia areata, and inflammatory myopathies. Exemplary infectious diseases include HIV and hepatitis B.

In some embodiments, the disease is cancer. The methods and uses can comprise administering a therapeutically effective amount of any of the herein disclosed modified hIL-2 protein-antibody conjugates to the subject to thereby treat the cancer. In some aspects, the cancer is melanoma. In some aspects, the cancer is non-small cell lung carcinoma.

EXAMPLES

The following examples are provided to further describe some of the embodiments disclosed herein. The examples are intended to illustrate, not to limit, the disclosed embodiments.

General Methods

Protocol A. Flow Cytometry Screen for Binding of Anti-hPD-1 Antibodies or Anti-hPD-1 Antibody-Attenuated hIL-2 Fusions to Human PD-1

To test for binding to hPD-1, antibodies and antibody-attenuated hIL-2 fusion proteins were characterized in full titration curves. A Jurkat cell line was transfected with a mammalian vector which encoded amino acids 1-185 of

human PD-1 (SEQ ID NO: 346) to stably express the extracellular domain and a portion of the transmembrane domain of human PD-1, and this transfected cell line was used to determine binding of anti-hPD-1 antibodies. Jurkat+hPD-1 cells were washed and added to 96-well plates at 100,000 cells per well in FACS buffer (PBS, 0.2% Heat-inactivated Fetal Bovine Serum). Cells were blocked with 1:50 dilution of human FcR Block (Miltenyi) for 10 minutes at 4° C. and washed with FACS buffer.

Antibodies or antibody-attenuated hIL-2 immunoconjugates (fusion proteins) were serially diluted six-fold in FACS buffer for an 8-point curve and added to human PD-1 expressing Jurkat cells for 1 hour on ice in 100 μ L volume. Cells were washed and re-suspended in FACS buffer containing 1:40 dilution of Allophycocyanin conjugated anti-human IgG Fc monoclonal antibody. Cells were washed once more, re-suspended in FACS buffer containing 1:1000 dilution of Sytox Green (Thermo Fisher) and flow cytometric analysis was conducted on the BD FACS Canto II, BD Celesta or BD Fortessa (BD Biosciences) flow cytometers. The geometric mean fluorescent intensity (gMFI) was calculated using FlowJo software version 10. Half maximal effective concentration (EC₅₀) values were calculated from the gMFI of the Allophycocyanin signal across the titrated concentrations using GraphPad Prism 7 software. Protocol B. Flow Cytometry Competition Screen for Binding of Anti-hPD-1 Antibodies or Anti-hPD-1 Antibody-Attenuated hIL-2 Fusions to Human PD-1

Antibodies and antibody-attenuated hIL-2 fusion proteins were tested for the ability to bind human PD-1 in the presence of a saturating concentration of anti-hPD-1 #1-mIgG2b-N297A (sequence comprising the heavy and light chain variable region sequences of nivolumab, clone 5C4, as described in U.S. Patent Pub. No. US 2009/0217401A1, formatted onto a murine IgG2b-N297A background) (SEQ ID NOs: 348 and 349) or anti-hPD-1 #2-mIgG2b-N297A (sequence comprising the heavy and light chain variable region sequences of pembrolizumab (clone 109A-H/K09A-L-11) as described in Int'l Pub. No. WO2008/156712A1, formatted onto a murine IgG2b-N297A background) (SEQ ID NOs: 350 and 351).

Antibodies or antibody-attenuated hIL-2 fusion proteins were serially diluted six-fold for an 8-point titration curve with and without saturating amounts of 10 μ M anti-hPD-1 #1-mIgG2b-N297A or anti-hPD-1 #2-mIgG2b-N297A. Briefly, Jurkat cells stably expressing hPD-1 (as described in Protocol A above) were washed and re-suspended in FACS buffer containing 1:50 dilution of human FcR Blocking reagent. Cells were incubated at 4° C. for 10 minutes and washed. Cells were then re-suspended in 100 μ L volume with anti-hPD-1 #1-mIgG2b-N297A or anti-hPD-1 #2-mIgG2b-N287A diluted in FACS buffer to 10 μ M and incubated at 4° C. for one hour. Cells were washed and incubated with test antibodies or antibody-attenuated hIL-2 fusion proteins serially diluted six-fold for an 8-point curve in 100 μ L volume for one hour at 4° C. To detect bound test anti-hPD-1 antibodies or anti-hPD-1-attenuated hIL-2 fusion proteins, cells were washed again and incubated with 1:40 dilution of Allophycocyanin-conjugated anti-human IgG Fc monoclonal antibody for 45 minutes on ice. Cells were washed and re-suspended in FACS buffer containing 1:1000 dilution of Sytox Green (Thermo Fisher). To generate a comparison, Jurkat cells stably expressing human PD-1 were incubated with only the titrated test antibodies or antibody-attenuated hIL-2 fusion proteins (without anti-hPD-1 #1-mIgG2b-N297A or anti-hPD-1 #2-mIgG2b-N297A) and subsequently with 1:40 dilution of Allophycocyanin-conjugated anti-human IgG Fc secondary. As a control, the variable regions of anti-hPD-1 #1 and anti-hPD-1 #2 were cloned into hIgG4 frameworks and were assessed with and without the addition of anti-hPD-1 #1-mIgG2b-N297A or anti-hPD-1 #2-mIgG2b-N297A. Flow cytometry was carried out on the BD Canto II, BD Celesta, or BD Fortessa (BD Biosciences) flow cytometers and gMFI was calculated using FlowJo software version 10. EC₅₀ values were calculated from the gMFI of the Allophycocyanin signal across the titrated concentrations using GraphPad Prism 7 software.

Protocol C. Cell-Based Screen for Characterization of Non-Antagonist Anti-hPD-1 Antibodies or Anti-hPD-1 Antibody-Attenuated hIL-2 Fusions

Human PD-1 antibodies and anti-hPD-1-attenuated hIL-2 fusion proteins were characterized for the ability to block hPD-1 from binding to ligand hPD-L1 (SEQ ID NO: 584). Anti-hPD-1 antibodies and anti-hPD-1-attenuated hIL-2 fusion proteins were either characterized as an antagonist or non-antagonist using an in vitro cell-based human PD-1/PD-L1 blockade bioassay (Promega, Cat #J1255). This co-culture assay utilized two cell lines: FCyR11b artificial Antigen Presenting Cells/Chinese Ovary Hamster K1 (aAPC/CHO-K1) and Jurkat Effector cells. aAPC/CHO K1 cells stably express both human PD-L1 ligand and a cell surface protein to activate cognate T cell receptors (TCRs) while Jurkat Effector cells express hPD-1 and a luciferase reporter under the control of Nuclear Factor of Activated T cells response element (NFAT-RE). When these cells are co-cultured in the presence of a non-antagonistic antibody, hPD-1/hPD-L1 interaction inhibits TCR signaling and no luminescence is detected. In the presence of an antibody that antagonizes hPD-1 interaction with hPD-L1 (SEQ ID NO: 584), the inhibitory signal is disrupted and luminescence is detected.

The thaw-and-use assay was performed according to manufacturer's instructions. In short, aAPC/CHO-K1 cells were first thawed and plated at 30,000 cells per well in flat-bottom 96-well plates for 18 hours at 37° C. in a 5% CO₂ incubator. After cells had adhered, the media was removed and 200 nM or 1000 nM test antibodies or antibody-attenuated hIL-2 fusion proteins were diluted in 40 μ L assay buffer (RPMI 1640 medium+1% FBS) and added to the aAPC/CHO-K1 cells. A human IgG4 isotype control monoclonal antibody which targeted Keyhole Limpet Hemocyanin (KLH) clone C3 (SEQ ID NOs: 585 and 586) was used as a negative control. Jurkat effector cells expressing hPD-1 were added at 24,000 cells per well in 40 μ L volume. The final concentration of fixed antibodies tested was 100 nM or 500 nM. In some examples, a range of concentrations of anti-hPD-11 or anti-hPD-1-attenuated hIL-2 fusion proteins were tested in this co-culture assay, with the top concentration in a five-fold titration series of 500 nM (FIG. 7).

The co-culture assay was incubated at 37° C. in a 5% CO₂ incubator for an additional 18-20 hours. To read the luminescence signal, plates were allowed to come to room temperature, and 80 μ L of the Bio-Glo™ reagent was added to each well. The plates were incubated for 15 minutes in the dark at room temperature and luminescence was read on a Victor X luminometer (Perkin Elmer). Relative luminescence units (RLU) were averaged for each triplicate and graphed using GraphPad Prism 7 software.

Protocol D. In Vitro Phosphorylated STAT5 Assay to Test Attenuation of hIL-2 Variants

The level of attenuation of hIL-2 receptor activation activity of antibody-attenuated hIL-2 fusion proteins was characterized using a phosphorylated STAT5 assay. Variants

were tested in both hIL-2 responsive human natural killer NK-92 cells and engineered human erythroleukemic TF1 cells. The NK-92 cell line naturally expresses the high-affinity hIL-2 receptor (IL-2R $\alpha\beta\gamma$) at physiologic levels, while the TF1 cell line that naturally expresses the IL-2R γ (SEQ ID NO: 352) was engineered to also stably express human CD122 (IL-2RB) (SEQ ID NO: 353) for expression of the intermediate affinity hIL-2 receptor complex (IL-2R $\beta\gamma$). This TF1+IL-2R β stable cell line does not express the IL-2R α (SEQ ID NO: 354). Both NK-92 and TF1+IL-2R β cell lines were used to assess the level of attenuation of IL-2 potency in these cell-based potency assays as fixed concentration screens and full titration curves.

To perform the fixed concentration screen, 100,000 NK-92 cells or TF1+IL-2R β cells were plated into 96 wells in 50 μ L of fresh growth medium lacking human IL-2 cytokine and incubated overnight at 37° C. in a CO₂ incubator. After 15-16 hours, human IL-2 starved cells were treated with 25.7 nM recombinant hIL-2 (denoted as rhIL-2) (SEQ ID NO: 345) or test antibody-attenuated hIL-2 fusion proteins for the NK-92 cell assay, or with 33.3 nM hIL-2 or test hIL-2 variants for the TF1+IL-2R β cell assay. Cells were incubated at 37° C., 5% CO₂ for 10 minutes. Cells were fixed with Cytofix Buffer (BD Biosciences) for 10 minutes at 37° C. and then permeabilized after treatment with Perm Buffer III (BD Biosciences) for 30 minutes on ice. hIL-2-dependent Stat5 phosphorylation was detected after staining fixed and permeabilized cells with Alexa Fluor-647 conjugated anti-Stat5 antibody (BD Biosciences) at 0.5 μ L per sample for 45 minutes at room temperature in the dark. Cells were washed and reagents were diluted in BD Pharmingen Buffer (BD Biosciences). Stained cells were acquired on a FACS-Celesta cytometer (BD Biosciences) and analyzed using FlowJo software version 10.7.2. The assays were performed in cohorts but normalized using the rhIL-2 for each plate. The degree of attenuation of selected antibody-attenuated hIL-2 fusion proteins were evaluated in an 8-point, 6-fold serially titrated curve ranging from 1200 nM to 7 pM on both NK-92 and TF1+IL-2R β cell lines. The procedure for the pStat5 curves was performed in the same manner as the method described above. EC₅₀ values were calculated from the geometric mean fluorescent intensity (gMFI) across the titrated concentrations using GraphPad Prism 7 software. The fold change in activity from rhIL-2 was calculated by dividing the EC₅₀ values for the variants by the EC₅₀ of hIL-2.

Protocol E. In Vitro Cell-Based Proliferation Assay to Test Attenuation of Antibody-Attenuated hIL-2 Fusion Proteins

The antibody-attenuated hIL-2 fusion proteins were also tested for attenuated hIL-2 activity in hIL-2 dependent cell proliferation assays. 10,000 NK-92 cells (expressing the high affinity receptor hIL-2R $\alpha\beta\gamma$) or TF1+IL-2R β cells (expressing the intermediate affinity receptor hIL-2R $\beta\gamma$) suspended in 50 μ L of fresh growth medium without hIL-2 cytokine were plated per well in 96-well U-bottom cell culture plate. Eight point, 6-fold serial titrations of antibody-attenuated hIL-2 fusion proteins with a highest concentration of 996 nM were diluted in fresh media and overlaid on cells in wells. Cells were incubated at 37° C. in a 5% CO₂ incubator for 3 days for TF1+IL-2R β cells or 4 days for NK-92 cells. To measure proliferation, Cell-Titer-Glo (Promega) was added to wells, incubated for 10 minutes at room temperature and luminescence was read for 0.1 second per well using a VictorX Multilabel Plate Reader (Perkin Elmer). EC₅₀ values were calculated from the relative luminescence units (RLU) across the titrated concentrations using GraphPad Prism 7 software. The fold change in

activity from rhIL-2 was calculated by dividing the EC₅₀ values for the variants by the EC₅₀ of hIL-2. The assays were performed in cohorts but normalized using the rhIL-2 EC₅₀ value for each plate.

Example 1: Optimization of Antibody-Attenuated hIL-2 Fusion Protein Variants and Determination of their hIL-2 Activity on the Intermediate and High-Affinity hIL-2 Receptor Complexes

In order to determine the optimal structures for an antibody-attenuated hIL-2 fusion protein, non-attenuated hIL-2 was fused to an anti-DNase I antibody (clone 1H3) designated as 1H3-hIgG1 (SEQ ID NO: 379, SEQ ID NO: 374) in the antibody variable region in a variety of ways as illustrated in FIG. 1. Variations included the hIL-2 fused at the N-terminus of the human anti-DNase I antibody (clone 1H3) immunoglobulin hIgG1 heavy chain or human kappa light chain via a direct fusion (df) denoted as hIL-2 Nterm light chain df (SEQ ID NO: 379, SEQ ID NO: 356), hIL-2 Nterm heavy chain df (SEQ ID NO: 358, SEQ ID NO: 374) or six amino acid linker (L6) (SEQ ID NO: 355) denoted as hIL-2 Nterm light chain L6 fusion (SEQ ID NO: 379, SEQ ID NO: 357) and hIL-2 Nterm heavy chain L6 fusion (SEQ ID NO: 359, SEQ ID NO: 374). Variations in which the hIL-2 moiety was fused to the C-terminus of both the heavy chains and light chains via df or L6 were also created and denoted as hIL-2 Cterm heavy chain df (SEQ ID NO: 360, SEQ ID NO: 374), hIL-2 Cterm heavy chain L6 fusion (SEQ ID NO: 361, SEQ ID: 374), hIL-2 Cterm light chain df (SEQ ID NO: 379, SEQ ID NO: 362), hIL-2 Cterm light chain L6 fusion (SEQ ID NO: 379, SEQ ID NO: 363). Further variations were generated in which a CD25/IL-2R α extracellular domain (amino acids 1-164) (SEQ ID NO: 126) was fused to the N-terminus or C-terminus of the heavy chains or the kappa light chains to interfere with the binding of the IL-2 to CD25 of the IL-2 receptor (FIG. 2). In these constructs, human CD25 extracellular domain (amino acids 1-164) (SEQ ID NO: 126) was fused to human IL-2 via a 20 amino acid linker (L20) (SEQ ID NO: 364), which was then directly fused or fused via an L6 linker (SEQ ID NO: 355) to 1H3-hIgG1 heavy chain or light chain at the N terminus: hCD25-L20-hIL-2 Nterm heavy chain df (SEQ ID NO: 365, SEQ ID NO: 374), hCD25-L20-hIL-2 Nterm heavy chain L6 fusion (SEQ ID NO: 366, SEQ ID NO: 374), hCD25-L20-hIL-2 Nterm light chain df (SEQ ID NO: 379, SEQ ID NO: 367), hCD25-L20-hIL-2 Nterm light chain L6 fusion (SEQ ID NO: 379, SEQ ID NO: 368). Lastly, a final set of variants in which the CD25/IL-2R α extracellular domain moiety (SEQ ID NO: 126) fused to the C-terminus of the heavy chain and kappa light chains were created: hCD25-L20-hIL-2 Cterm heavy chain df (SEQ ID NO: 369, SEQ ID NO: 374), hCD25-L20-hIL-2 Cterm heavy chain L6 fusion (SEQ ID NO: 370, SEQ ID NO: 374), hCD25-L20-hIL-2 Cterm light chain df (SEQ ID NO: 379, SEQ ID NO: 371), hCD25-L20-hIL-2 Cterm light chain L6 fusion (SEQ ID NO: 379, SEQ ID NO: 372). These antibody-hIL-2 fusion proteins were produced, expressed, and Protein-A purified using standard techniques. The 16 N- or C-terminus and linker variants described above were evaluated in an in vitro cell-based phosphorylated STAT5 assay using an 8-point, 6-fold serial titration, as described in Protocol D.

Table 1 summarizes the EC₅₀ calculated over the 8-point, 6-fold serially titrated curves using the geometric mean fluorescence intensity (gMFI) calculated by the FlowJo version 10 software. The fold change from rhIL-2 was also calculated for each variant as a measurement of the level of

attenuation as compared to the activity of the rhIL-2 positive control. Some EC₅₀ values were unable to be calculated by the GraphPad Prism 7 software and were marked as Not Calculated (NC); however, based on dose-titration curves there was no attenuation for these variants.

Fusions of the hIL-2 moiety to the N-terminus or C-terminus of the immunoglobulin heavy chain resulted in no reduction in IL-2 activity when compared to rhIL-2 on cell lines expressing the high-affinity hIL-2 receptor (NK-92) or intermediate-affinity hIL-2 receptor (TF1+IL-2RB). The direct fusion (df) of hIL-2 to the antibody component of the fusion protein resulted in no change in IL-2 activity when

compared with fusion employing a six amino acid linker (L6) between the IL-2 and antibody components. Similarly, fusions of the IL-2 component to the heavy chain or light chain of the antibody component resulted in no change in IL-2 activity when compared to rhIL-2. All N- or C-terminus and linker fusion protein variants in which the hCD25/hIL-2R α moiety was fused to hIL-2 were predicted to exhibit reduced binding of the fusion protein to the CD25 of the hIL-2 receptor on cells. Experimentally these constructs exhibited strongly attenuated hIL-2 activity (by at least 45-fold) on the high affinity IL-2 receptor (NK-92) and by 18-fold on the intermediate hIL-2 receptor (TF1+IL-2RB).

TABLE 1

| pSTAT5 EC ₅₀ and fold change on fusion protein domain variants | | | | | | | |
|---|-----------------------|---------------------------------|---------------------------------|--|--|--|---|
| HC or LC Component Of Fusion Protein | HC and LC SEQ ID NOS: | pSTAT5 EC ₅₀ (NK-92) | Fold change from rhIL-2 (NK-92) | Attenuation based on dose-titration curves (NK-92) | pSTAT5 EC ₅₀ (TF1 + IL-2R β) | Fold change from rhIL-2 (TF1 + IL-2R β) | Attenuation based on dose-titration curves (TF1 + IL-2R β) |
| hIL-2 Nterm heavy chain df | 358, 374 | <0.1 ^a | 1 ^a | Not Attenuated | 1.11 | 2 | Not Attenuated |
| hIL-2 Nterm heavy chain L6 fusion | 359, 374 | NC ^a | NC ^a | Not Attenuated | 0.19 | 0 | Not Attenuated |
| hIL-2 Nterm light chain df | 379, 356 | <0.1 ^a | 1 ^a | Not Attenuated | 0.52 | 1 | Not Attenuated |
| hIL-2 Nterm light chain L6 fusion | 379, 357 | <0.1 ^a | 0 ^a | Not Attenuated | 0.13 | 0 | Not Attenuated |
| hIL-2 Cterm heavy chain df | 360, 374 | <0.1 ^a | 0 ^a | Not Attenuated | <0.1 | 0 | Not Attenuated |
| hIL-2 Cterm heavy chain L6 fusion | 361, 374 | NC ^a | NC ^a | Not Attenuated | <0.1 | 0 | Not Attenuated |
| hIL-2 Cterm light chain df | 379, 362 | NC ^a | NC ^a | Not Attenuated | 1.15 | 1 | Not Attenuated |
| hIL-2 Cterm light chain L6 fusion | 379, 363 | <0.1 ^a | 0 ^a | Not Attenuated | 0.25 | 0 | Not Attenuated |
| hCD25-L20-hIL-2 Nterm heavy chain df | 365, 374 | 7.42 | 1052 | Attenuated | 190.50 ^a | 314 ^a | Attenuated |
| hCD25-L20-hIL-2 Nterm heavy chain L6 fusion | 366, 374 | 2.24 | 318 | Attenuated | 10.70 | 18 | Attenuated |
| hCD25-L20-hIL-2 Nterm light chain df | 379, 367 | 106.80 | 15149 | Attenuated | 328.50 ^a | 542 ^a | Attenuated |
| hCD25-L20-hIL-2 Nterm light chain L6 fusion | 379, 368 | 4.45 | 631 | Attenuated | 27.88 | 46 | Attenuated |
| hCD25-L20-hIL-2 Cterm heavy chain df | 369, 374 | 1.89 | 149 | Attenuated | 93.89 ^a | 104 ^a | Attenuated |
| hCD25-L20-hIL-2 Cterm heavy chain L6 fusion | 370, 374 | 6.09 | 479 | Attenuated | 90.53 ^a | 101 ^a | Attenuated |
| hCD25-L20-hIL-2 Cterm light chain df | 379, 371 | 0.58 | 45 | Attenuated | 156.90 ^a | 174 ^a | Attenuated |
| hCD25-L20-hIL-2 Cterm light chain L6 fusion | 379, 372 | 1.76 | 138 | Attenuated | 221.90 ^a | 247 ^a | Attenuated |

NC = Not Calculated;

^a = Fold change is an estimate only since a full four parameter logistic curve was not reached

Example 2: Antibody-Attenuated hIL-2 Fusion Protein Variant Production and Determination of their Binding Kinetics to Recombinant Human CD25 and/or Human CD122

Since there was no reduction in hIL-2 activity in the various N-terminus or C-terminus immunoglobulin heavy chain fusion proteins, the hIL-2 Cterm heavy chain L6 fusion (SEQ ID NOs: 361, 374), designated as “1H3-hIgG1-L6-hIL-2”, was used as the base construct for antibody-attenuated-hIL-2 fusion protein variants with substitutions in the hIL-2 moiety. Single, double and/or multiple amino acid substitutions were introduced into selected residues of human IL-2 in order to investigate the role those residues play in the recognition of either human CD25/IL-2R α and/or human CD122/IL-2R β or CD132/IL-2R γ (human IL-2R subunits). Over three hundred antibody-attenuated hIL-2 fusion protein variants with substitutions in the hIL-2 moiety were generated and evaluated in 6 rounds. These variants were first screened using a flow-based phosphorylated STAT5 (pSTAT5) assay at a fixed concentration on IL-2 dependent cell lines (NK-92 and TF1+IL-2RB) as well as in dose-titration curves. Phosphorylated STAT5 is a downstream signal of IL-2 activity and was used as a snapshot measurement of IL-2 potency. IL-2 dependent cell proliferation assays were also performed to measure IL-2 activity over a period of 3-4 days. Criteria for attenuated hIL-2 selection included: (1) reduced IL-2 potency on both NK-92 and TF1+IL-2R β cell lines with greater than 50% agonist activity on both cell lines; and (2) moderate-to-high production yield.

Human anti-DNase I antibody-hIL-2 fusion proteins were generated by fusing the human IL-2 or the human IL-2 variants (SEQ ID NOs: 1-344, 377, 378, and 575) to the C-terminus of a human anti-DNase I antibody (clone 1H3, having a human IgG1 isotype) heavy chain via the L6 linker, which were combined with the hIgG1 light chain (1H3-hkappa LC; SEQ ID NO: 374) to generate the 1H3-hIgG1-L6-hIL-2 fusion proteins (provided in Table 28). Mouse anti-yellow fever virus antibody-hIL-2 fusion proteins were also generated by fusing human IL-2 variants to the C-terminus of a mouse anti-yellow fever virus antibody (clone 2D12, having a mouse IgG1 isotype) heavy chain with a D265A substitution for decreased immune effector function via the L6 linker, which were combined with the 2D12-mIgG1 light chain (2D12-mKappa LC; SEQ ID NO: 376) to generate the 2D12-mIgG1-D265A-L6-hIL-2 fusion proteins (provided in Table 28). Some of these mouse anti-yellow fever virus antibody-hIL-2 fusion proteins were formatted onto a human IgG1 constant region and were generated in the same manner as described above using, which was combined with 2D12-hKappa light chain (2D12-hKappa LC; SEQ ID NO: 573). Iterations of IL-2 amino acid substitutions were performed in six rounds, designated Groups 1 to 6. 1H3-hIgG1-L6-hIL-2, 2D12-mIgG1-D265A-L6-hIL-2, and 2D12-hIgG1-L6-hIL-2 fusion proteins were produced, expressed, and Protein-A purified using standard techniques.

Group 1 contained an initial series of only 2D12-mIgG1-D265A-L6-hIL-2 or 2D12-hIgG1-L6-hIL-2 fusion proteins which comprised a substitution or combination of substitutions in human IL-2 which were predicted to be involved in binding to only one of the IL-2 receptor subunits CD25/IL-2R α , CD122/IL-2R β , or CD132/IL-2R γ . The fusion proteins in this group included the following substitutions to IL-2 predicted to modulate binding to CD25/IL-2R α : F42K (SEQ ID NO: 1), V69A (SEQ ID NO: 2), V69E (SEQ ID

NO: 3), V69F (SEQ ID NO: 4), V69G (SEQ ID NO: 5), V69H (SEQ ID NO: 6), V69I (SEQ ID NO: 7), V69K (SEQ ID NO: 8), V69L (SEQ ID NO: 9), V69M (SEQ ID NO: 10), V69N (SEQ ID NO: 11), V69S (SEQ ID NO: 12), V69T (SEQ ID NO: 13), V69W (SEQ ID NO: 14), V69Y (SEQ ID NO: 15), V69R (SEQ ID NO: 581), (F42K/F44K) (SEQ ID NO: 16), (F44K/Y45R) (SEQ ID NO: 17), (F42K/V69R) (SEQ ID NO: 18), (Y45R/V69R) (SEQ ID NO: 19), (F42K/F44K/Y45R) (SEQ ID NO: 20), (F42A/Y45A/L72G) (SEQ ID NO: 574), (R38A/F42K/Y45R) (SEQ ID NO: 21), (R38E/F42K/Y45R) (SEQ ID NO: 22), (K43E/F42K/Y45R) (SEQ ID NO: 23), (K43T/F42K/Y45R) (SEQ ID NO: 24), (F42K/Y45R/E62A) (SEQ ID NO: 25), (P65R/F42K/Y45R) (SEQ ID NO: 26), (P65S/F42K/Y45R) (SEQ ID NO: 27), (V69A/F42K/Y45R) (SEQ ID NO: 28), (V69D/F42K/Y45R) (SEQ ID NO: 29), or (V69R/F42K/Y45R) (SEQ ID NO: 30). The substitutions in this group included the following substitutions predicted to modulate binding to CD122/IL-2R β : D20A (SEQ ID NO: 31), D20N (SEQ ID NO: 32), D20K (SEQ ID NO: 33), N88A (SEQ ID NO: 34), N88G (SEQ ID NO: 35), N88H (SEQ ID NO: 36), N88K (SEQ ID NO: 37), (D20A/D84A) (SEQ ID NO: 38), (D20A/E15A) (SEQ ID NO: 39), (D20A/E95A) (SEQ ID NO: 40), (D20A/N88A) (SEQ ID NO: 41), (D20A/S87A) (SEQ ID NO: 42), (D84A/N88A) (SEQ ID NO: 43), (E15A/N88A) (SEQ ID NO: 44), or (S87A/N88A) (SEQ ID NO: 45). Group 1 also included the following substitutions to IL-2 predicted to modulate IL-2 binding to CD132/IL-2R γ : Q126L (SEQ ID NO: 377) or Q126E (SEQ ID NO: 378). The IL-2 substitutions studied in Group 1 were not predicted to modulate binding to more than one of the IL-2 receptor subunits.

Group 2 contained a series of 1H3-hIgG1-L6-hIL-2 fusion proteins which comprised one or more substitutions in human IL-2 which were predicted to be involved in CD25/IL-2R α binding only. The fusion proteins in this group included the following substitutions to IL-2 predicted to modulate binding to CD25/IL-2R α : R38A (SEQ ID NO: 46), R38D (SEQ ID NO: 47), R38E (SEQ ID NO: 48), R38Q (SEQ ID NO: 49), F42R (SEQ ID NO: 50), F42A (SEQ ID NO: 51), F42D (SEQ ID NO: 52), F42H (SEQ ID NO: 53), K43A (SEQ ID NO: 54), K43E (SEQ ID NO: 55), K43Q (SEQ ID NO: 56), Y45A (SEQ ID NO: 57), Y45K (SEQ ID NO: 58), Y45S (SEQ ID NO: 59), Y45R (SEQ ID NO: 60), E61A (SEQ ID NO: 61), E61R (SEQ ID NO: 62), E61K (SEQ ID NO: 63), E62A (SEQ ID NO: 64), E62R (SEQ ID NO: 65), E62K (SEQ ID NO: 66), E62Y (SEQ ID NO: 67), E68Y (SEQ ID NO: 68), E68A (SEQ ID NO: 69), E68K (SEQ ID NO: 70), E68R (SEQ ID NO: 71), E68L (SEQ ID NO: 72), L72Y (SEQ ID NO: 73), L72R (SEQ ID NO: 74), L72A (SEQ ID NO: 75), L72D (SEQ ID NO: 76), L72H (SEQ ID NO: 77), L72F (SEQ ID NO: 78), (R38D/E61R) (SEQ ID NO: 79), (R38D/E61R/K43E) (SEQ ID NO: 80), or (T3A/F42A/Y45A/L72G/C125A) (SEQ ID NO: 81). The substitution T3A was introduced into the IL-2 amino acid sequence to remove the predicted O-linked glycosylation site on human IL-2 (see for example Int'l Pub. No. WO2012/107417) and the substitution C125A was introduced into the IL-2 amino acid sequence to remove an unpaired cysteine residue (see for example Int'l Pub. No. WO2018/184964). The IL-2 substitutions studied in Group 2 were predicted to not modulate IL-2 binding to CD132/IL-2R γ , nor were these substitutions predicted to modulate binding to more than one of the IL-2 receptor subunits.

Group 3 contained a series of 1H3-hIgG1-L6-hIL-2 fusion proteins which comprised one or more substitutions in human IL-2 which were predicted to be involved in

CD122/IL-2R β binding only. The fusion proteins in this group included the following substitutions to IL-2 predicted to modulate binding to CD122/IL-2RB: E15A (SEQ ID NO: 82), E15R (SEQ ID NO: 83), E15K (SEQ ID NO: 84), H16A (SEQ ID NO: 85), H16Y (SEQ ID NO: 86), H16E (SEQ ID NO: 87), L19A (SEQ ID NO: 88), D20I (SEQ ID NO: 89), D20S (SEQ ID NO: 90), D20H (SEQ ID NO: 91), D20T (SEQ ID NO: 92), D20W (SEQ ID NO: 93), D20Y (SEQ ID NO: 94), D20R (SEQ ID NO: 95), D20F (SEQ ID NO: 96), R81A (SEQ ID NO: 97), D84A (SEQ ID NO: 98), D84R (SEQ ID NO: 99), D84K (SEQ ID NO: 100), S87A (SEQ ID NO: 101), N88Y (SEQ ID NO: 102), N88D (SEQ ID NO: 103), N88R (SEQ ID NO: 104), N88E (SEQ ID NO: 10⁵), N88F (SEQ ID NO: 106), N88I (SEQ ID NO: 107), 192A (SEQ ID NO: 108), 192Y (SEQ ID NO: 109), 192S (SEQ ID NO: 110), 192F (SEQ ID NO: 111), 192R (SEQ ID NO: 112), 192D (SEQ ID NO: 113), 192E (SEQ ID NO: 114), E95A (SEQ ID NO: 115), E95R (SEQ ID NO: 116), E95K (SEQ ID NO: 117), (D20Y/H16E) (SEQ ID NO: 118), (D20Y/H16A) (SEQ ID NO: 119), (D20Y/H16Y) (SEQ ID NO: 120), (D20Y/192A) (SEQ ID NO: 121), (D20Y/192S) (SEQ ID NO: 122), (D20Y/192R) (SEQ ID NO: 123), (D20Y/E95R) (SEQ ID NO: 124), or (D20Y/E95A) (SEQ ID NO: 125).

Group 4 contained a series of fusion proteins containing the 1H3-hIgG1-L6-hIL-2 HC fused to a CD25/IL-2R α extracellular domain moiety (SEQ ID NO: 126), a 20 amino acid linker (L20) (SEQ ID NO: 364), and human IL-2 variants comprising one or more substitutions to residues predicted to be involved in binding to CD122/IL-2R β . The fusion proteins in this group included the following substitutions to IL-2 predicted to modulate binding to CD122/IL-2R β : E15A (SEQ ID NO: 82), D20I (SEQ ID NO: 89), D20S (SEQ ID NO: 90), D20H (SEQ ID NO: 91), D20W (SEQ ID NO: 93), D20Y (SEQ ID NO: 94), D20R (SEQ ID NO: 95), D20F (SEQ ID NO: 96), D84K (SEQ ID NO: 100), S87A (SEQ ID NO: 101), N88Y (SEQ ID NO: 102), N88D (SEQ ID NO: 103), N88R (SEQ ID NO: 104), N88E (SEQ ID NO: 10⁵), N88F (SEQ ID NO: 106), N88I (SEQ ID NO: 107), 192A (SEQ ID NO: 108), E95A (SEQ ID NO: 115), or E95K (SEQ ID NO: 117). The antibody-attenuated hIL-2 fusion proteins in this group are denoted as 1H3-hIgG1-L6-hCD25 (1-164)-L20-hIL-2.

Group 5 contained a series of 1H3-hIgG1-L6-hIL-2 which comprised a combination of substitutions in IL-2 which were predicted to be involved in binding of IL-2 to CD25/IL-2R α and to CD122/IL-2R β or CD132/IL-2R γ . In addition, some variants had a deletion in the first three amino acids at the N-terminus of the hIL-2 moiety (Δ 1-3APT). The fusion proteins in Group 5 included the following substitutions to IL-2 predicted to modulate IL-2 binding to CD25/IL-2R α and to CD122/IL-2R β : (F42D/D20A) (SEQ ID NO: 127), (F42R/D20A) (SEQ ID NO: 128), (F42K/D20A) (SEQ ID NO: 129), (F42A/D20A) (SEQ ID NO: 130), (F42H/D20A) (SEQ ID NO: 131), (Y45R/D20A) (SEQ ID NO: 132), (Y45K/D20A) (SEQ ID NO: 133), (R38N/D20A) (SEQ ID NO: 134), (R38G/D20A) (SEQ ID NO: 135), (R38H/D20A) (SEQ ID NO: 136), (R38I/D20A) (SEQ ID NO: 137), (R38L/D20A) (SEQ ID NO: 138), (R38M/D20A) (SEQ ID NO: 139), (R38F/D20A) (SEQ ID NO: 140), (R38P/D20A) (SEQ ID NO: 141), (R38S/D20A) (SEQ ID NO: 142), (R38T/D20A) (SEQ ID NO: 143), (R38W/D20A) (SEQ ID NO: 144), (R38Y/D20A) (SEQ ID NO: 145), (R38V/D20A) (SEQ ID NO: 146), (R38A/D20A) (SEQ ID NO: 147), (R38Q/D20A) (SEQ ID NO: 148), (D20A/R38E) (SEQ ID NO: 149), (R38D/D20A) (SEQ ID NO: 150), (K43E/D20A) (SEQ ID NO: 151), (E61A/D20A) (SEQ ID

NO: 152), (E62A/D20A) (SEQ ID NO: 153), (E62Y/D20A) (SEQ ID NO: 154), (L72D/D20A) (SEQ ID NO: 155), (L72H/D20A) (SEQ ID NO: 156), (L72R/D20A) (SEQ ID NO: 157), (F42D/192D) (SEQ ID NO: 158), (F42R/192D) (SEQ ID NO: 159), (F42H/192D) (SEQ ID NO: 160), (F42A/192D) (SEQ ID NO: 161), (H16A/F42A) (SEQ ID NO: 575), (K43E/192D) (SEQ ID NO: 162), (Y45R/192D) (SEQ ID NO: 163), (Y45K/192D) (SEQ ID NO: 164), (E62A/192D) (SEQ ID NO: 165), (E62Y/192D) (SEQ ID NO: 166), (L72D/192D) (SEQ ID NO: 167), (L72H/192D) (SEQ ID NO: 168), (L72R/192D) (SEQ ID NO: 169), (R38D/192D) (SEQ ID NO: 170), (R38E/192D) (SEQ ID NO: 171), (R38Q/192D) (SEQ ID NO: 172), (R38A/192D) (SEQ ID NO: 173), (R38E/N88R) (SEQ ID NO: 174), (R38E/D84R) (SEQ ID NO: 175), (R38E/D84K) (SEQ ID NO: 176), (F42A/Y45R/D20A) (SEQ ID NO: 177), (F42H/Y45R/D20A) (SEQ ID NO: 178), (R38D/E61R/D20A) (SEQ ID NO: 179), (R38E/E61R/D20A) (SEQ ID NO: 180), (R38Q/E61R/D20A) (SEQ ID NO: 181), (R38A/E61R/D20A) (SEQ ID NO: 182), (R38A/D20A/E95A) (SEQ ID NO: 183), (D20A/E95A/R38D) (SEQ ID NO: 184), (D20A/E95A/R38E) (SEQ ID NO: 185), (D20A/E95A/R38Q) (SEQ ID NO: 186), (D20A/E95A/F42R) (SEQ ID NO: 187), (D20A/E95A/F42A) (SEQ ID NO: 188), (D20A/E95A/F42D) (SEQ ID NO: 189), (D20A/E95A/F42H) (SEQ ID NO: 190), (D20A/E95A/F42K) (SEQ ID NO: 191), (D20A/E95A/K43A) (SEQ ID NO: 192), (D20A/E95A/K43E) (SEQ ID NO: 193), (D20A/E95A/K43Q) (SEQ ID NO: 194), (D20A/E95A/Y45A) (SEQ ID NO: 195), (D20A/E95A/Y45K) (SEQ ID NO: 196), (D20A/E95A/Y45S) (SEQ ID NO: 197), (D20A/E95A/Y45R) (SEQ ID NO: 198), (D20A/E95A/E61A) (SEQ ID NO: 199), (D20A/E95A/E62A) (SEQ ID NO: 200), (D20A/E95A/E62R) (SEQ ID NO: 201), (D20A/E95A/E62K) (SEQ ID NO: 202), (D20A/E95A/E62Y) (SEQ ID NO: 203), (D20A/E95A/E68Y) (SEQ ID NO: 204), (D20A/E95A/E68A) (SEQ ID NO: 205), (D20A/E95A/E68L) (SEQ ID NO: 206), (D20A/E95A/L72Y) (SEQ ID NO: 207), (D20A/E95A/L72R) (SEQ ID NO: 208), (D20A/E95A/L72A) (SEQ ID NO: 209), (D20A/E95A/L72D) (SEQ ID NO: 210), (D20A/E95A/L72H) (SEQ ID NO: 211), (D20A/E95A/L72F) (SEQ ID NO: 212), (F42K/Y45R/D20A/S87A) (SEQ ID NO: 213), (F42K/Y45R/D20A/E95A) (SEQ ID NO: 214), (D20A/R38E/C125A) (SEQ ID NO: 215), (T3A/D20A/R38E) (SEQ ID NO: 216), (T3A/D20A/R38E/C125A) (SEQ ID NO: 217), (Δ -3APT/D20A/R38E) (SEQ ID NO: 218), or (Δ -3APT/D20A/R38E/C125A) (SEQ ID NO: 219). The fusion proteins in Group 5 included the following substitutions to IL-2 predicted to modulate IL-2 binding to CD25/IL-2R α and to CD132/IL-2R: (R38E/Q22A) (SEQ ID NO: 220), (R38E/T123A) (SEQ ID NO: 221), (R38E/1129A) (SEQ ID NO: 222), (R38E/S130A) (SEQ ID NO: 223), (R38E/Q126A) (SEQ ID NO: 224), (R38E/Q126D) (SEQ ID NO: 225), (R38E/Q126V) (SEQ ID NO: 226), (R38E/Q22A/S130A) (SEQ ID NO: 227), (F42K/Y45R/Q126D) (SEQ ID NO: 228), or (D20A/E95A/Q126D) (SEQ ID NO: 229). Mutations to the hIL-2 sequence for Group 5 antibody-attenuated hIL-2 fusion proteins in which the numbering is according to IL-2 sequence are listed in SEQ ID NO: 127-229 and 575.

Group 6 contained a series of 1H3-hIgG1-L6-hIL-2 fusion proteins which comprised a combination of substitutions in human IL-2 which were predicted to be involved in binding of IL-2 to CD25/IL-2R α and to CD122/IL-2R β , but not to CD132/IL-2R γ . The fusion proteins in Group 6 included the following combination of substitutions in IL-2 predicted to modulate IL-2 binding to CD25/IL-2R α and

CD122/IL-2R β : (D20A/E61R) (SEQ ID NO: 230), (D20A/E61N) (SEQ ID NO: 231), (D20A/E61D) (SEQ ID NO: 232), (D20A/E61Q) (SEQ ID NO: 233), (D20A/E61G) (SEQ ID NO: 234), (D20A/E61H) (SEQ ID NO: 235), (D20A/E61I) (SEQ ID NO: 236), (D20A/E61L) (SEQ ID NO: 237), (D20A/E61K) (SEQ ID NO: 238), (D20A/E61M) (SEQ ID NO: 239), (D20A/E61F) (SEQ ID NO: 240), (D20A/E61P) (SEQ ID NO: 241), (D20A/E61S) (SEQ ID NO: 242), (D20A/E61T) (SEQ ID NO: 243), (D20A/E61W) (SEQ ID NO: 244), (D20A/E61Y) (SEQ ID NO: 245), (D20A/E61V) (SEQ ID NO: 246), (D20A/F42N) (SEQ ID NO: 247), (D20A/F42Q) (SEQ ID NO: 248), (D20A/F42E) (SEQ ID NO: 249), (D20A/F42G) (SEQ ID NO: 250), (D20A/F42I) (SEQ ID NO: 251), (D20A/F42L) (SEQ ID NO: 252), (D20A/F42M) (SEQ ID NO: 253), (D20A/F42P) (SEQ ID NO: 254), (D20A/F42S) (SEQ ID NO: 255), (D20A/F42T) (SEQ ID NO: 256), (D20A/F42W) (SEQ ID NO: 257), (D20A/F42Y) (SEQ ID NO: 258), (D20A/F42V) (SEQ ID NO: 259), (D20A/Y45A) (SEQ ID NO: 260), (D20A/Y45N) (SEQ ID NO: 261), (D20A/Y45D) (SEQ ID NO: 262), (D20A/Y45Q) (SEQ ID NO: 263), (D20A/Y45E) (SEQ ID NO: 264), (D20A/Y45G) (SEQ ID NO: 265), (D20A/Y45H) (SEQ ID NO: 266), (D20A/Y45I) (SEQ ID NO: 267), (D20A/Y45L) (SEQ ID NO: 268), (D20A/Y45M) (SEQ ID NO: 269), (D20A/Y45F) (SEQ ID NO: 270), (D20A/Y45P) (SEQ ID NO: 271), (D20A/Y45S) (SEQ ID NO: 272), (D20A/Y45T) (SEQ ID NO: 273), (D20A/Y45W) (SEQ ID NO: 274), (D20A/Y45V) (SEQ ID NO: 275), (192D/F42N) (SEQ ID NO: 276), (192D/F42Q) (SEQ ID NO: 277), (192D/F42E) (SEQ ID NO: 278), (192D/F42G) (SEQ ID NO: 279), (192D/F42I) (SEQ ID NO: 280), (192D/F42L) (SEQ ID NO: 281), (192D/F42K) (SEQ ID NO: 282), (192D/F42M) (SEQ ID NO: 283), (192D/F42P) (SEQ ID NO: 284), (192D/F42S) (SEQ ID NO: 285), (192D/F42T) (SEQ ID NO: 286), (192D/F42W) (SEQ ID NO: 287), (192D/F42Y) (SEQ ID NO: 288), (192D/F42V) (SEQ ID NO: 289), (192D/Y45A) (SEQ ID NO: 290), (192D/Y45N) (SEQ ID NO: 291), (192D/Y45D) (SEQ ID NO: 292), (192D/Y45Q) (SEQ ID NO: 293), (192D/Y45E) (SEQ ID NO: 294), (192D/Y45G) (SEQ ID NO: 295), (192D/Y45H) (SEQ ID NO: 296), (192D/Y45I) (SEQ ID NO: 297), (192D/Y45L) (SEQ ID NO: 298), (192D/Y45M) (SEQ ID NO: 299), (192D/Y45F) (SEQ ID NO: 300), (192D/Y45P) (SEQ ID NO: 301), (192D/Y45S) (SEQ ID NO: 302), (192D/Y45T) (SEQ ID NO: 303), (192D/Y45W) (SEQ ID NO: 304), (192D/Y45V) (SEQ ID NO: 305),

(R38E/D20H) (SEQ ID NO: 306), (R38E/D20S) (SEQ ID NO: 307), (F42A/N88R) (SEQ ID NO: 308), (F42A/N88D) (SEQ ID NO: 309), (R38E/D84A) (SEQ ID NO: 310), (R38E/D84N) (SEQ ID NO: 311), (R38E/D84Q) (SEQ ID NO: 312), (R38E/D84E) (SEQ ID NO: 313), (R38E/D84G) (SEQ ID NO: 314), (R38E/D84H) (SEQ ID NO: 315), (R38E/D84I) (SEQ ID NO: 316), (R38E/D84L) (SEQ ID NO: 317), (R38E/D84M) (SEQ ID NO: 318), (R38E/D84F) (SEQ ID NO: 319), (R38E/D84P) (SEQ ID NO: 320), (R38E/D84S) (SEQ ID NO: 321), (R38E/D84T) (SEQ ID NO: 322), (R38E/D84W) (SEQ ID NO: 323), (R38E/D84Y) (SEQ ID NO: 324), (R38E/D84V) (SEQ ID NO: 325), (R38E/192A) (SEQ ID NO: 326), (R38E/192R) (SEQ ID NO: 327), (R38E/192N) (SEQ ID NO: 328), (R38E/192Q) (SEQ ID NO: 329), (R38E/192E) (SEQ ID NO: 330), (R38E/192G) (SEQ ID NO: 331), (R38E/192H) (SEQ ID NO: 332), (R38E/192L) (SEQ ID NO: 333), (R38E/192K) (SEQ ID NO: 334), (R38E/192M) (SEQ ID NO: 335), (R38E/192F) (SEQ ID NO: 336), (R38E/192P) (SEQ ID NO: 337), (R38E/192S) (SEQ ID NO: 338), (R38E/192T) (SEQ ID NO: 339), (R38E/192W) (SEQ ID NO: 340), (R38E/192Y) (SEQ ID NO: 341), (R38E/192V) (SEQ ID NO: 342), (R38E/H16E) (SEQ ID NO: 343), or (R38K/D20A) (SEQ ID NO: 344). Mutations to the hIL-2 sequence for Group 6 antibody-attenuated hIL-2 fusion proteins in which the numbering is according to IL-2 sequence is listed in SEQ ID NO: 230-344.

The binding kinetics of some purified 1H3-hIgG1-L6-hIL-2 variant proteins for individual recombinant human CD25 and human CD122 were determined using bio-layer interferometry (BLI). Briefly, binding experiments were performed using an Octet Red96 instrument (Pall ForteBio) at 25° C. C-terminal poly-histidine tagged human CD25 and human CD122 extracellular domains were captured onto anti-His2 sensors (Pall ForteBio). Receptor loaded sensors were dipped into a 7-point serial 3-fold dilution of each 1H3-hIgG-L6-hIL-2 variant, starting at a top concentration of 300 nM. 1H3-hIgG1-L6-hIL-2 fusion proteins were diluted into an assay buffer consisting of phosphate buffered saline (PBMS) supplemented with 0.1% BSA, 0.02% Tween-20 (pH 7.2). Loaded sensors were regenerated using 10 mM Glycine buffer (pH 1.7). Kinetic constants were calculated using a monovalent binding model.

Table 2 documents the association constant (k_{on}), dissociation constant (k_{off}), and equilibrium constant (K_D) of 74 immunoglobulin-hIL-2 fusion protein variants bound to recombinant human CD25 or recombinant human CD122.

TABLE 2

| Binding kinetics of 1H3-hIgG-L6-hIL-2 fusion proteins to recombinant human CD25 or CD122 by Octet BLI | | | | | |
|---|----------------------------|---|-----------|-----------------|-----------------|
| 1H3-hIgG1-L6-hIL-2 fusion proteins | SEQ ID NO of hIL-2 variant | Predicted receptor sub-unit targeted by IL-2 substitution | K_D (M) | k_{on} (1/Ms) | k_{off} (1/s) |
| 1H3-hIgG1-L6-hIL-2 WT | 345 | N/A | 3.20E-10 | 5.90E+05 | 1.90E-04 |
| 1H3-hIgG1-L6-hIL-2 (E15A) | 82 | CD122 | 2.04E-09 | 1.15E+05 | 2.35E-04 |
| 1H3-hIgG1-L6-hIL-2 (E15R) | 83 | CD122 | 3.41E-09 | 9.48E+04 | 3.23E-04 |
| 1H3-hIgG1-L6-hIL-2 (E15K) | 84 | CD122 | 1.39E-09 | 1.71E+05 | 2.37E-04 |
| 1H3-hIgG1-L6-hIL-2 (H16A) | 85 | CD122 | 1.68E-09 | 1.71E+05 | 2.87E-04 |
| 1H3-hIgG1-L6-hIL-2 (H16Y) | 86 | CD122 | 1.46E-09 | 1.50E+05 | 2.20E-04 |
| 1H3-hIgG1-L6-hIL-2 (H16E) | 87 | CD122 | 1.40E-09 | 1.57E+05 | 2.20E-04 |

TABLE 2-continued

| Binding kinetics of 1H3-hIgG-L6-hIL-2 fusion proteins to recombinant human CD25 or CD122 by Octet BLI | | | | | |
|---|----------------------------|---|---------------------|-----------------|-----------------|
| 1H3-hIgG1-L6-hIL-2 fusion proteins | SEQ ID NO of hIL-2 variant | Predicted receptor sub-unit targeted by IL-2 substitution | K_D (M) | k_{on} (1/Ms) | k_{off} (1/s) |
| 1H3-hIgG1-L6-hIL-2 (L19A) | 88 | CD122 | 1.76E-09 | 2.03E+05 | 3.57E-04 |
| 1H3-hIgG1-L6-hIL-2 (D20I) | 89 | CD122 | 1.16E-09 | 1.70E+05 | 1.98E-04 |
| 1H3-hIgG1-L6-hIL-2 (D20S) | 90 | CD122 | 6.24E-10 | 1.74E+05 | 1.09E-04 |
| 1H3-hIgG1-L6-hIL-2 (D20H) | 91 | CD122 | 1.13E-09 | 1.88E+05 | 2.12E-04 |
| 1H3-hIgG1-L6-hIL-2 (D20W) | 93 | CD122 | 1.01E-09 | 1.87E+05 | 1.90E-04 |
| 1H3-hIgG1-L6-hIL-2 (D20Y) | 94 | CD122 | 1.42E-09 | 1.51E+05 | 2.14E-04 |
| 1H3-hIgG1-L6-hIL-2 (D20R) | 95 | CD122 | 1.21E-09 | 1.44E+05 | 1.75E-04 |
| 1H3-hIgG1-L6-hIL-2 (D20F) | 96 | CD122 | 1.57E-09 | 1.75E+05 | 2.75E-04 |
| 1H3-hIgG1-L6-hIL-2 (R38A) | 46 | CD25 | 5.55E-09 | 1.82E+05 | 1.01E-03 |
| 1H3-hIgG1-L6-hIL-2 (R38D) | 47 | CD25 | 1.86E-09 | 8.84E+05 | 1.64E-03 |
| 1H3-hIgG1-L6-hIL-2 (R38E) | 48 | CD25 | 8.74E-09 | 3.31E+05 | 2.89E-03 |
| 1H3-hIgG1-L6-hIL-2 (R38Q) | 49 | CD25 | 6.33E-09 | 4.83E+05 | 3.05E-03 |
| 1H3-hIgG1-L6-hIL-2 (F42R) | 50 | CD25 | 2.63E-09 | 1.59E+06 | 4.20E-03 |
| 1H3-hIgG1-L6-hIL-2 (F42A) | 51 | CD25 | 9.25E-09 | 9.89E+05 | 9.15E-03 |
| 1H3-hIgG1-L6-hIL-2 (F42D) | 52 | CD25 | 4.51E-09 | 1.70E+06 | 7.64E-03 |
| 1H3-hIgG1-L6-hIL-2 (F42H) | 53 | CD25 | 6.84E-09 | 8.23E+05 | 5.63E-03 |
| 1H3-hIgG1-L6-hIL-2 (K43A) | 54 | CD25 | 4.79E-09 | 2.59E+05 | 1.24E-03 |
| 1H3-hIgG1-L6-hIL-2 (K43E) | 55 | CD25 | 5.66E-09 | 4.52E+05 | 2.56E-03 |
| 1H3-hIgG1-L6-hIL-2 (K43Q) | 56 | CD25 | 2.28E-09 | 4.49E+05 | 1.02E-03 |
| 1H3-hIgG1-L6-hIL-2 (Y45A) | 57 | CD25 | 3.66E-09 | 4.29E+05 | 1.57E-03 |
| 1H3-hIgG1-L6-hIL-2 (Y45K) | 58 | CD25 | 9.03E-09 | 5.22E+05 | 4.71E-03 |
| 1H3-hIgG1-L6-hIL-2 (Y45S) | 59 | CD25 | 2.45E-09 | 5.05E+05 | 1.24E-03 |
| 1H3-hIgG1-L6-hIL-2 (Y45R) | 60 | CD25 | 1.96E-09 | 6.46E+05 | 1.27E-03 |
| 1H3-hIgG1-L6-hIL-2 (E61A) | 61 | CD25 | 7.00E-09 | 3.21E+05 | 2.25E-03 |
| 1H3-hIgG1-L6-hIL-2 (E61R) | 62 | CD25 | 8.84E-09 | 1.22E+06 | 1.08E-02 |
| 1H3-hIgG1-L6-hIL-2 (E61K) | 63 | CD25 | 1.56E-08 | 3.16E+05 | 4.94E-03 |
| 1H3-hIgG1-L6-hIL-2 (E62A) | 64 | CD25 | 1.23E-08 | 3.79E+05 | 4.67E-03 |
| 1H3-hIgG1-L6-hIL-2 (E62R) | 65 | CD25 | No binding observed | | |
| 1H3-hIgG1-L6-hIL-2 (E62K) | 66 | CD25 | No binding observed | | |
| 1H3-hIgG1-L6-hIL-2 (E62Y) | 67 | CD25 | 1.55E-08 | 2.91E+05 | 4.50E-03 |
| 1H3-hIgG1-L6-hIL-2 (E68Y) | 68 | CD25 | 8.18E-09 | 1.80E+05 | 1.47E-03 |
| 1H3-hIgG1-L6-hIL-2 (E68A) | 69 | CD25 | 4.49E-09 | 1.45E+05 | 6.52E-04 |
| 1H3-hIgG1-L6-hIL-2 (E68K) | 70 | CD25 | 9.63E-09 | 2.54E+05 | 2.44E-03 |
| 1H3-hIgG1-L6-hIL-2 (E68R) | 71 | CD25 | 1.16E-08 | 2.54E+05 | 2.96E-03 |
| 1H3-hIgG1-L6-hIL-2 (E68L) | 72 | CD25 | 8.62E-09 | 1.02E+05 | 8.82E-04 |
| 1H3-hIgG1-L6-hIL-2 (I92R) | 112 | CD122 | 2.54E-09 | 1.08E+05 | 2.76E-04 |

TABLE 2-continued

| Binding kinetics of 1H3-hIgG-L6-hIL-2 fusion proteins to recombinant human CD25 or CD122 by Octet BLI | | | | | |
|---|----------------------------|---|---------------------|-----------------|-----------------|
| 1H3-hIgG1-L6-hIL-2 fusion proteins | SEQ ID NO of hIL-2 variant | Predicted receptor sub-unit targeted by IL-2 substitution | K_D (M) | k_{on} (1/Ms) | k_{off} (1/s) |
| 1H3-hIgG1-L6-hIL-2 (I92D) | 113 | CD122 | 7.94E-09 | 4.95E+04 | 3.93E-04 |
| 1H3-hIgG1-L6-hIL-2 (I92E) | 114 | CD122 | 2.41E-09 | 8.54E+04 | 2.06E-04 |
| 1H3-hIgG1-L6-hIL-2 (E95A) | 115 | CD122 | 3.11E-09 | 1.47E+05 | 4.58E-04 |
| 1H3-hIgG1-L6-hIL-2 (E95R) | 116 | CD122 | 2.29E-09 | 1.14E+05 | 2.61E-04 |
| 1H3-hIgG1-L6-hIL-2 (E95K) | 117 | CD122 | 3.25E-09 | 1.25E+05 | 4.07E-04 |
| 1H3-hIgG1-L6-hIL-2 (F42K/Y45R/D20A/S87A) | 213 | CD25 + CD122 | 3.25E-08 | 1.24E+05 | 4.05E-03 |
| 1H3-hIgG1-L6-hIL-2 (F42K/Y45R/D20A/E95A) | 214 | CD25 + CD122 | No binding observed | | |
| 1H3-hIgG1-L6-hIL-2 (F42K/Y45R/Q126D) | 228 | CD25 + CD132 | No binding observed | | |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/Q126D) | 229 | CD122 + CD132 | 3.34E-09 | 4.87E+04 | 1.62E-04 |
| 1H3-hIgG1-L6-hIL-2 (R38D/E61R) | 79 | CD25 | No binding observed | | |
| 1H3-hIgG1-L6-hIL-2 (R38D/E61R/K43E) | 80 | CD25 | No binding observed | | |

Table 3 documents the association (k_{on}) constants, dissociation (k_{off}) constants, and equilibrium constants (K_D)³⁰ of 74 1H3-hIgG1-L6-hIL-2 fusion proteins bound to recombinant human CD122.

TABLE 3

| Binding kinetics of 1H3-hIgG-L6-hIL-2 fusion proteins to recombinant human CD122 by Octet BLI | | | | | |
|---|----------------------------|---|---------------------|-----------------|-----------------|
| 1H3-hIgG-L6-hIL-2 fusion proteins | SEQ ID NO of hIL-2 variant | Predicted receptor sub-unit targeted by IL-2 substitution | K_D (M) | k_{on} (1/Ms) | k_{off} (1/s) |
| 1H3-hIgG1-L6-hIL-2 WT | 345 ^a | N/A | 5.60E-09 | 7.00E+05 | 3.90E-03 |
| 1H3-hIgG1-L6-hIL-2 (E15A) | 82 ^b | CD122 | 8.89E-09 | 1.75E+05 | 1.56E-03 |
| 1H3-hIgG1-L6-hIL-2 (E15R) | 83 | CD122 | 3.69E-09 | 1.46E+05 | 5.38E-04 |
| 1H3-hIgG1-L6-hIL-2 (E15K) | 84 | CD122 | 3.56E-09 | 2.42E+05 | 8.62E-04 |
| 1H3-hIgG1-L6-hIL-2 (H16A) | 85 | CD122 | 1.78E-09 | 1.55E+06 | 2.76E-03 |
| 1H3-hIgG1-L6-hIL-2 (H16Y) | 86 | CD122 | 4.36E-09 | 9.97E+05 | 4.35E-03 |
| 1H3-hIgG1-L6-hIL-2 (H16E) | 87 | CD122 | No binding observed | | |
| 1H3-hIgG1-L6-hIL-2 (L19A) | 88 | CD122 | 1.03E-08 | 4.72E+05 | 4.87E-03 |
| 1H3-hIgG1-L6-hIL-2 (D20I) | 89 | CD122 | No binding observed | | |
| 1H3-hIgG1-L6-hIL-2 (D20S) | 90 | CD122 | No binding observed | | |
| 1H3-hIgG1-L6-hIL-2 (D20H) | 91 | CD122 | No binding observed | | |
| 1H3-hIgG1-L6-hIL-2 (D20W) | 93 | CD122 | No binding observed | | |
| 1H3-hIgG1-L6-hIL-2 (D20Y) | 94 | CD122 | No binding observed | | |
| 1H3-hIgG1-L6-hIL-2 (D20R) | 95 | CD122 | No binding observed | | |
| 1H3-hIgG1-L6-hIL-2 (D20F) | 96 | CD122 | No binding observed | | |
| 1H3-hIgG1-L6-hIL-2 (R38A) | 46 | CD25 | 1.38E-08 | 2.08E+05 | 2.87E-03 |

TABLE 3-continued

Binding kinetics of 1H3-hIgG-L6-hIL-2 fusion proteins to recombinant human CD122 by Octet BLI

| 1H3-hIgG-L6-hIL-2 fusion proteins | SEQ ID NO of hIL-2 variant | Predicted receptor sub-unit targeted by IL-2 substitution | K_D (M) | k_{on} (1/Ms) | k_{off} (1/s) |
|-----------------------------------|----------------------------|---|---------------------|-----------------|-----------------|
| 1H3-hIgG1-L6-hIL-2 (R38D) | 47 | CD25 | 2.20E-09 | 4.28E+05 | 9.42E-04 |
| 1H3-hIgG1-L6-hIL-2 (R38E) | 48 | CD25 | 5.81E-09 | 4.64E+05 | 2.69E-03 |
| 1H3-hIgG1-L6-hIL-2 (R38Q) | 49 | CD25 | 1.01E-09 | 2.81E+05 | 2.84E-04 |
| 1H3-hIgG1-L6-hIL-2 (F42R) | 50 | CD25 | 5.47E-09 | 5.42E+05 | 2.96E-03 |
| 1H3-hIgG1-L6-hIL-2 (F42A) | 51 | CD25 | 5.97E-09 | 4.19E+05 | 2.50E-03 |
| 1H3-hIgG1-L6-hIL-2 (F42D) | 52 | CD25 | 1.04E-08 | 2.38E+05 | 2.46E-03 |
| 1H3-hIgG1-L6-hIL-2 (F42H) | 53 | CD25 | 6.33E-09 | 4.45E+05 | 2.81E-03 |
| 1H3-hIgG1-L6-hIL-2 (K43A) | 54 | CD25 | 1.03E-08 | 2.85E+05 | 2.94E-03 |
| 1H3-hIgG1-L6-hIL-2 (K43E) | 55 | CD25 | 5.47E-09 | 3.65E+05 | 2.00E-03 |
| 1H3-hIgG1-L6-hIL-2 (K43Q) | 56 | CD25 | 4.21E-09 | 5.14E+05 | 2.17E-03 |
| 1H3-hIgG1-L6-hIL-2 (Y45A) | 57 | CD25 | 4.93E-09 | 4.51E+05 | 2.22E-03 |
| 1H3-hIgG1-L6-hIL-2 (Y45K) | 58 | CD25 | 6.56E-09 | 3.55E+05 | 2.33E-03 |
| 1H3-hIgG1-L6-hIL-2 (Y45S) | 59 | CD25 | 6.96E-09 | 5.07E+05 | 3.53E-03 |
| 1H3-hIgG1-L6-hIL-2 (Y45R) | 60 | CD25 | 7.58E-09 | 4.36E+05 | 3.31E-03 |
| 1H3-hIgG1-L6-hIL-2 (E61A) | 61 | CD25 | 1.34E-08 | 3.13E+05 | 4.18E-03 |
| 1H3-hIgG1-L6-hIL-2 (E61R) | 62 | CD25 | 1.30E-08 | 4.56E+05 | 5.91E-03 |
| 1H3-hIgG1-L6-hIL-2 (E61K) | 63 | CD25 | 1.56E-08 | 3.16E+05 | 4.94E-03 |
| 1H3-hIgG1-L6-hIL-2 (E62A) | 64 | CD25 | 1.23E-08 | 3.79E+05 | 4.67E-03 |
| 1H3-hIgG1-L6-hIL-2 (E62R) | 65 | CD25 | No binding observed | | |
| 1H3-hIgG1-L6-hIL-2 (E62K) | 66 | CD25 | No binding observed | | |
| 1H3-hIgG1-L6-hIL-2 (E62Y) | 67 | CD25 | 1.55E-08 | 2.91E+05 | 4.50E-03 |
| 1H3-hIgG1-L6-hIL-2 (E68Y) | 68 | CD25 | 8.18E-09 | 1.80E+05 | 1.47E-03 |
| 1H3-hIgG1-L6-hIL-2 (E68A) | 69 | CD25 | 4.49E-09 | 1.45E+05 | 6.52E-04 |
| 1H3-hIgG1-L6-hIL-2 (E68K) | 70 | CD25 | 1.05E-08 | 2.02E+05 | 2.12E-03 |
| 1H3-hIgG1-L6-hIL-2 (E68R) | 71 | CD25 | 8.51E-09 | 2.27E+05 | 1.93E-03 |
| 1H3-hIgG1-L6-hIL-2 (E68L) | 72 | CD25 | 2.72E-09 | 7.79E+04 | 2.12E-04 |
| 1H3-hIgG1-L6-hIL-2 (L72Y) | 73 | CD25 | 6.39E-09 | 1.94E+05 | 1.24E-03 |
| 1H3-hIgG1-L6-hIL-2 (L72R) | 74 | CD25 | 1.96E-08 | 3.07E+04 | 6.01E-04 |
| 1H3-hIgG1-L6-hIL-2 (L72A) | 75 | CD25 | 9.08E-09 | 1.47E+05 | 1.34E-03 |
| 1H3-hIgG1-L6-hIL-2 (L72D) | 76 | CD25 | 9.52E-09 | 1.57E+05 | 1.50E-03 |
| 1H3-hIgG1-L6-hIL-2 (L72H) | 77 | CD25 | 9.03E-09 | 1.65E+05 | 1.49E-03 |
| 1H3-hIgG1-L6-hIL-2 (L72F) | 78 | CD25 | 5.04E-09 | 2.28E+05 | 1.15E-03 |
| 1H3-hIgG1-L6-hIL-2 (R81A) | 97 | CD122 | 7.08E-09 | 2.20E+05 | 1.56E-03 |
| 1H3-hIgG1-L6-hIL-2 (D84A) | 98 | CD122 | No binding observed | | |
| 1H3-hIgG1-L6-hIL-2 (D84R) | 99 | CD122 | 1.88E-08 | 4.73E+05 | 8.88E-03 |
| 1H3-hIgG1-L6-hIL-2 (S87A) | 101 | CD122 | 7.09E-09 | 3.31E+05 | 2.34E-03 |

TABLE 3-continued

Binding kinetics of 1H3-hIgG-L6-hIL-2 fusion proteins to recombinant human CD122 by Octet BLI

| 1H3-hIgG-L6-hIL-2 fusion proteins | SEQ ID NO of hIL-2 variant | Predicted receptor sub-unit targeted by IL-2 substitution | K_D (M) | k_{on} (1/Ms) | k_{off} (1/s) |
|--|----------------------------|---|---------------------|-----------------|-----------------|
| 1H3-hIgG1-L6-hIL-2 (N88Y) | 102 | CD122 | No binding observed | | |
| 1H3-hIgG1-L6-hIL-2 (N88D) | 103 | CD122 | No binding observed | | |
| 1H3-hIgG1-L6-hIL-2 (N88R) | 104 | CD122 | No binding observed | | |
| 1H3-hIgG1-L6-hIL-2 (N88E) | 105 | CD122 | No binding observed | | |
| 1H3-hIgG1-L6-hIL-2 (N88F) | 106 | CD122 | No binding observed | | |
| 1H3-hIgG1-L6-hIL-2 (N88I) | 107 | CD122 | No binding observed | | |
| 1H3-hIgG1-L6-hIL-2 (I92A) | 108 | CD122 | 3.38E-09 | 1.95E+06 | 6.58E-03 |
| 1H3-hIgG1-L6-hIL-2 (I92Y) | 109 | CD122 | 1.23E-08 | 4.53E+05 | 5.57E-03 |
| 1H3-hIgG1-L6-hIL-2 (I92S) | 110 | CD122 | No binding observed | | |
| 1H3-hIgG1-L6-hIL-2 (I92F) | 111 | CD122 | 5.45E-09 | 1.03E+05 | 5.59E-04 |
| 1H3-hIgG1-L6-hIL-2 (I92R) | 112 | CD122 | No binding observed | | |
| 1H3-hIgG1-L6-hIL-2 (I92D) | 113 | CD122 | No binding observed | | |
| 1H3-hIgG1-L6-hIL-2 (I92E) | 114 | CD122 | 1.62E-09 | 9.33E+05 | 1.51E-03 |
| 1H3-hIgG1-L6-hIL-2 (E95A) | 115 | CD122 | 8.17E-09 | 2.87E+05 | 2.35E-03 |
| 1H3-hIgG1-L6-hIL-2 (E95R) | 116 | CD122 | No binding observed | | |
| 1H3-hIgG1-L6-hIL-2 (E95K) | 117 | CD122 | 3.81E-09 | 6.58E+05 | 2.51E-03 |
| 1H3-hIgG1-L6-hIL-2 (F42K/Y45R/D20A/S87A) | 213 | CD25 + CD122 | No binding observed | | |
| 1H3-hIgG1-L6-hIL-2 (F42K/Y45R/D20A/E95A) | 214 | CD25 + CD122 | No binding observed | | |
| 1H3-hIgG1-L6-hIL-2 (F42K/Y45R/Q126D) | 228 | CD25 + CD132 | 9.16E-09 | 3.75E+05 | 3.44E-03 |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/Q126D) | 229 | CD122 + CD132 | No binding observed | | |
| 1H3-hIgG1-L6-hIL-2 (R38D/E61R) | 79 | CD25 | 1.29E-08 | 3.68E+05 | 4.73E-03 |
| 1H3-hIgG1-L6-hIL-2 (R38D/E61R/K43E) | 80 | CD25 | 7.47E-09 | 4.52E+05 | 3.38E-03 |

^aSEQ ID NO: 345 corresponds to wild type hIL-2.^bSEQ ID NO: 57 is attenuated IL-2 sequence only.

Example 3: Testing for Attenuation for the High-Affinity and Intermediate-Affinity hIL-2 Receptor with a Fixed Concentration Cell-Based Potency pSTAT5 Screen

The attenuation of antibody-attenuated hIL-2 fusion proteins described in Example 2 was tested in a fixed concentration pSTAT5 screen using the NK-92 (expressing the high affinity hIL-2 receptor) and TF1+IL-2R β (expressing the intermediate affinity hIL-2 receptor) cell lines as described in Protocol D. Tables 4-8 list the fold change of geometric mean fluorescent intensity (gMFI) of antibody-attenuated hIL-2 fusion proteins from free cytokine wild-type rhIL-2, a measurement of reduction of IL-2 activity. For the fixed concentration screen, the fold change was calculated by dividing the gMFI of the rhIL-2 by the gMFI of the variants. For experiments with full titration curves, fold change from rhIL-2 was calculated by dividing the EC₅₀ values for the rhIL-2 by the EC₅₀ of variants. Fold change was rounded to the nearest whole number. A reduced gMFI in both NK-92

and TF1+IL-2R β cell lines when compared to the gMFI resulting from rhIL-2 was indicative of attenuation of IL-2 activity at both the high- and intermediate-affinity receptors. Group 1 variants described in Example 2 were not tested in the fixed concentration cell-based potency pSTAT5 screen.

Each variant tested was also assessed for IL-2 agonistic activity and characterized either as a full or partial IL-2 agonist, or having no IL-2 activity (inactive). 1H3-hIgG1-L6-hIL-2 fusion protein dose-titration curves that reached the maximal gMFI level exhibited by the rhIL-2 positive control were considered to be antibody-attenuated hIL-2 fusion protein with full agonist activity. Partial agonist activity was calculated as a percentage of full activity using rhIL-2 maximal gMFI as 100%. Antibody-attenuated hIL-2 fusion protein with less than 10% of the rhIL-2 maximal gMFI at the highest concentration of 1200 nM were considered to have no agonist activity (inactive). Some EC₅₀ values and level of attenuation could not be accurately calculated using the GraphPad Prism 7 software since activity did not reach a maximum and accordingly these values are an estimate.

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pSTAT5 fixed concentration results demonstrated that while some single residue substitutions attenuated IL-2 activity on the high-affinity cell line (NK-92), a combination of substitutions which modulated binding to both the alpha chain and the beta chain or both the alpha chain and gamma chain were required to substantially attenuate IL-2 activity on the high affinity IL-2 receptor (more than 20-fold attenuation from recombinant hIL-2).

TABLE 4

| Fold change from rhIL-2 in a fixed concentration pSTAT5 screen on 1H3-hlgG1-L6-hIL-2 fusion proteins from Group 2 | | | |
|---|----------------------------|--------------------------------|---------------------------------------|
| Variants | SEQ ID NO of hIL-2 variant | Fold change from hIL-2 (NK-92) | Fold change from hIL-2 (TF1 + IL-2Rβ) |
| 1H3-hlgG1-L6-hIL-2 (R38D) | 47 | 7 | 1 |
| 1H3-hlgG1-L6-hIL-2 (R38E) | 48 | 12 | 1 |
| 1H3-hlgG1-L6-hIL-2 (R38Q) | 49 | 1 | 1 |
| 1H3-hlgG1-L6-hIL-2 (F42R) | 50 | 7 | 1 |
| 1H3-hlgG1-L6-hIL-2 (F42A) | 51 | 1 | 1 |
| 1H3-hlgG1-L6-hIL-2 (F42H) | 53 | 1 | 1 |
| 1H3-hlgG1-L6-hIL-2 (K43E) | 55 | 1 | 1 |
| 1H3-hlgG1-L6-hIL-2 (K43Q) | 56 | 1 | 1 |
| 1H3-hlgG1-L6-hIL-2 (Y45A) | 57 | 1 | 1 |
| 1H3-hlgG1-L6-hIL-2 (Y45K) | 58 | 1 | 1 |
| 1H3-hlgG1-L6-hIL-2 (Y45S) | 59 | 1 | 1 |
| 1H3-hlgG1-L6-hIL-2 (Y45R) | 60 | 10 | 1 |
| 1H3-hlgG1-L6-hIL-2 (E68Y) | 68 | 1 | 1 |
| 1H3-hlgG1-L6-hIL-2 (E68A) | 69 | 1 | 1 |
| 1H3-hlgG1-L6-hIL-2 (E68L) | 72 | 2 | 1 |
| 1H3-hlgG1-L6-hIL-2 (L72Y) | 73 | 1 | 1 |
| 1H3-hlgG1-L6-hIL-2 (L72A) | 75 | 1 | 1 |
| 1H3-hlgG1-L6-hIL-2 (L72F) | 78 | 1 | 1 |
| 1H3-hlgG1-L6-hIL-2 (R38D/E61R) | 79 | NT-1 | 1 |
| 1H3-hlgG1-L6-hIL-2 (R38D/E61R/K43E) | 80 | NT-1 | 1 |
| 1H3-hlgG1-L6-hIL-2 (T3A/F42A/Y45A/L72G/C125A) | 81 | 10 | 1 |

NT-1 = Already tested in pSTAT5 full titration first, no data for fixed concentration assay.

TABLE 5

| Fold change from rhIL-2 in a fixed concentration pSTAT5 screen on 1H3-hlgG1-L6-hIL-2 fusion proteins from Group 3 | | | |
|---|----------------------------|--------------------------------|----------------------------|
| Variants | SEQ ID NO of hIL-2 variant | Fold change from hIL-2 (NK-92) | Fold change (TF1 + IL-2Rβ) |
| 1H3-hlgG1-L6-hIL-2 (E15A) | 82 | 1 | 1 |
| 1H3-hlgG1-L6-hIL-2 (E15R) | 83 | 1 | 1 |
| 1H3-hlgG1-L6-hIL-2 (E15K) | 84 | 1 | 1 |
| 1H3-hlgG1-L6-hIL-2 (H16A) | 85 | 1 | 1 |
| 1H3-hlgG1-L6-hIL-2 (H16Y) | 86 | 1 | 1 |
| 1H3-hlgG1-L6-hIL-2 (H16E) | 87 | 1 | NT-1 |
| 1H3-hlgG1-L6-hIL-2 (L19A) | 88 | 1 | NT-1 |
| 1H3-hlgG1-L6-hIL-2 (D20I) | 89 | 12 | NT-1 |
| 1H3-hlgG1-L6-hIL-2 (D20S) | 90 | 4 | NT-1 |
| 1H3-hlgG1-L6-hIL-2 (D20H) | 91 | 10 | NT-1 |
| 1H3-hlgG1-L6-hIL-2 (D20W) | 93 | 16 | NT-1 |
| 1H3-hlgG1-L6-hIL-2 (D20Y) | 94 | 17 | NT-1 |
| 1H3-hlgG1-L6-hIL-2 (D20R) | 95 | 19 | NT-1 |
| 1H3-hlgG1-L6-hIL-2 (D20F) | 96 | 17 | NT-1 |
| 1H3-hlgG1-L6-hIL-2 (R81A) | 97 | 1 | 1 |
| 1H3-hlgG1-L6-hIL-2 (D84A) | 98 | 1 | NT-1 |
| 1H3-hlgG1-L6-hIL-2 (D84R) | 99 | 3 | NT-1 |
| 1H3-hlgG1-L6-hIL-2 (D84K) | 100 | 2 | NT-1 |
| 1H3-hlgG1-L6-hIL-2 (S87A) | 101 | 1 | 1 |
| 1H3-hlgG1-L6-hIL-2 (N88Y) | 102 | 22 | NT-1 |
| 1H3-hlgG1-L6-hIL-2 (N88D) | 103 | 2 | NT-1 |
| 1H3-hlgG1-L6-hIL-2 (N88R) | 104 | 3 | NT-1 |

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TABLE 5-continued

| Fold change from rhIL-2 in a fixed concentration pSTAT5 screen on 1H3-hlgG1-L6-hIL-2 fusion proteins from Group 3 | | | |
|---|----------------------------|--------------------------------|---------------------------------------|
| 5 Variants | SEQ ID NO of hIL-2 variant | Fold change from hIL-2 (NK-92) | Fold change from hIL-2 (TF1 + IL-2Rβ) |
| 10 1H3-hlgG1-L6-hIL-2 (N88E) | 105 | 10 | NT-1 |
| 1H3-hlgG1-L6-hIL-2 (N88F) | 106 | 19 | NT-1 |
| 1H3-hlgG1-L6-hIL-2 (N88I) | 107 | 9 | NT-1 |
| 1H3-hlgG1-L6-hIL-2 (I92A) | 108 | 1 | 1 |
| 1H3-hlgG1-L6-hIL-2 (I92Y) | 109 | 1 | NT-1 |
| 1H3-hlgG1-L6-hIL-2 (I92S) | 110 | 1 | NT-1 |
| 1H3-hlgG1-L6-hIL-2 (I92F) | 111 | 1 | 1 |
| 1H3-hlgG1-L6-hIL-2 (I92R) | 112 | 1 | NT-1 |
| 1H3-hlgG1-L6-hIL-2 (I92D) | 113 | 3 | NT-1 |
| 1H3-hlgG1-L6-hIL-2 (I92E) | 114 | 1 | 1 |
| 1H3-hlgG1-L6-hIL-2 (E95A) | 115 | 1 | 1 |
| 1H3-hlgG1-L6-hIL-2 (E95R) | 116 | 1 | NT-1 |
| 1H3-hlgG1-L6-hIL-2 (E95K) | 117 | 1 | 1 |
| 1H3-hlgG1-L6-hIL-2 (D20T) | 92 | 3 | 2 |
| 1H3-hlgG1-L6-hIL-2 (D20A) | 31 | 7 | 2 |
| 1H3-hlgG1-L6-hIL-2 (D20Y/H16E) | 118 | 6 | 4 |
| 1H3-hlgG1-L6-hIL-2 (D20Y/H16A) | 119 | 10 | 3 |
| 1H3-hlgG1-L6-hIL-2 (D20Y/H16Y) | 120 | 10 | 4 |
| 1H3-hlgG1-L6-hIL-2 (D20Y/192A) | 121 | 11 | 4 |
| 1H3-hlgG1-L6-hIL-2 (D20Y/192S) | 122 | 11 | 4 |
| 1H3-hlgG1-L6-hIL-2 (D20Y/192R) | 123 | 12 | 5 |
| 1H3-hlgG1-L6-hIL-2 (D20Y/E95R) | 124 | 12 | 5 |
| 1H3-hlgG1-L6-hIL-2 (D20Y/E95A) | 125 | 11 | 5 |
| 35 NT-1 = Already tested in pSTAT5 full titration first, no data for fixed concentration assay. | | | |

TABLE 6

| Fold change from rhIL-2 in a fixed concentration pSTAT5 screen on 1H3-hlgG1-L6-hIL-2 fusion proteins from Group 4 | | | |
|---|----------------------------|--------------------------------|---------------------------------------|
| 40 Variants | SEQ ID NO of hIL-2 variant | Fold change from hIL-2 (NK-92) | Fold change from hIL-2 (TF1 + IL-2Rβ) |
| 1H3-hlgG1-L6-hCD25(1-164)-L20-hIL-2 (E15A) | 82 | 17 | 1 |
| 1H3-hlgG1-L6-hCD25(1-164)-L20-hIL-2 (D20I) | 89 | 21 | 15 |
| 1H3-hlgG1-L6-hCD25(1-164)-L20-hIL-2 (D20S) | 90 | 2 | 14 |
| 1H3-hlgG1-L6-hCD25(1-164)-L20-hIL-2 (D20W) | 91 | 22 | 15 |
| 1H3-hlgG1-L6-hCD25(1-164)-L20-hIL-2 (D20H) | 93 | 23 | 15 |
| 1H3-hlgG1-L6-hCD25(1-164)-L20-hIL-2 (D20Y) | 94 | 23 | 16 |
| 1H3-hlgG1-L6-hCD25(1-164)-L20-hIL-2 (D20R) | 95 | 23 | 16 |
| 1H3-hlgG1-L6-hCD25(1-164)-L20-hIL-2 (D20F) | 96 | 23 | 18 |
| 1H3-hlgG1-L6-hCD25(1-164)-L20-hIL-2 (D84K) | 100 | 23 | 17 |
| 1H3-hlgG1-L6-hCD25(1-164)-L20-hIL-2 (S87A) | 101 | 17 | 2 |
| 1H3-hlgG1-L6-hCD25(1-164)-L20-hIL-2 (N88Y) | 102 | 23 | 18 |
| 1H3-hlgG1-L6-hCD25(1-164)-L20-hIL-2 (N88D) | 103 | 23 | 17 |

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TABLE 6-continued

| Fold change from rhIL-2 in a fixed concentration pSTAT5 screen on 1H3-hIgG1-L6-hIL-2 fusion proteins from Group 4 | | | |
|---|----------------------------|--------------------------------|---|
| Variants | SEQ ID NO of hIL-2 variant | Fold change from hIL-2 (NK-92) | Fold change from hIL-2 (TF1 + IL-2R β) |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (N88R) | 104 | 24 | 17 |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (N88E) | 105 | 25 | 18 |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (N88F) | 106 | 25 | 18 |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (N88I) | 107 | 25 | 20 |

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TABLE 6-continued

| Fold change from rhIL-2 in a fixed concentration pSTAT5 screen on 1H3-hIgG1-L6-hIL-2 fusion proteins from Group 4 | | | |
|---|----------------------------|--------------------------------|---|
| Variants | SEQ ID NO of hIL-2 variant | Fold change from hIL-2 (NK-92) | Fold change from hIL-2 (TF1 + IL-2R β) |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (I192A) | 108 | 15 | 3 |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (E95A) | 115 | 14 | 1 |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (E95K) | 117 | 25 | 8 |

TABLE 7

| Fold change from rhIL-2 in a fixed concentration pSTAT5 screen on 1H3-hIgG1-L6-hIL-2 fusion proteins from Group 5 | | | |
|---|----------------------------|--------------------------------|---|
| Variants | SEQ ID NO of hIL-2 variant | Fold change from hIL-2 (NK-92) | Fold change from hIL-2 (TF1 + IL-2R β) |
| 1H3-hIgG1-L6-hIL-2 (F42D/D20A) | 127 | 11 | 3 |
| 1H3-hIgG1-L6-hIL-2 (F42R/D20A) | 128 | 10 | 2 |
| 1H3-hIgG1-L6-hIL-2 (F42K/D20A) | 129 | 10 | 4 |
| 1H3-hIgG1-L6-hIL-2 (F42A/D20A) | 130 | 11 | 3 |
| 1H3-hIgG1-L6-hIL-2 (F42H/D20A) | 131 | 12 | 2 |
| 1H3-hIgG1-L6-hIL-2 (Y45R/D20A) | 132 | 11 | 1 |
| 1H3-hIgG1-L6-hIL-2 (Y45K/D20A) | 133 | 11 | 2 |
| 1H3-hIgG1-L6-hIL-2 (R38N/D20A) | 134 | 14 | 3 |
| 1H3-hIgG1-L6-hIL-2 (R38G/D20A) | 135 | 13 | 2 |
| 1H3-hIgG1-L6-hIL-2 (R38H/D20A) | 136 | 12 | 3 |
| 1H3-hIgG1-L6-hIL-2 (R38I/D20A) | 137 | 11 | 3 |
| 1H3-hIgG1-L6-hIL-2 (R38L/D20A) | 138 | 11 | 4 |
| 1H3-hIgG1-L6-hIL-2 (R38M/D20A) | 139 | 11 | 3 |
| 1H3-hIgG1-L6-hIL-2 (R38F/D20A) | 140 | 12 | 3 |
| 1H3-hIgG1-L6-hIL-2 (R38P/D20A) | 141 | 13 | 3 |
| 1H3-hIgG1-L6-hIL-2 (R38S/D20A) | 142 | 15 | 2 |
| 1H3-hIgG1-L6-hIL-2 (R38T/D20A) | 143 | 13 | 3 |
| 1H3-hIgG1-L6-hIL-2 (R38W/D20A) | 144 | 14 | 2 |
| 1H3-hIgG1-L6-hIL-2 (R38Y/D20A) | 145 | 14 | 3 |
| 1H3-hIgG1-L6-hIL-2 (R38V/D20A) | 146 | 12 | 3 |
| 1H3-hIgG1-L6-hIL-2 (R38A/D20A) | 147 | 13 | 3 |
| 1H3-hIgG1-L6-hIL-2 (R38Q/D20A) | 148 | 14 | 3 |
| 1H3-hIgG1-L6-hIL-2 (R38E/D20A) | 149 | 15 | 3 |
| 1H3-hIgG1-L6-hIL-2 (R38D/D20A) | 150 | 15 | 3 |
| 1H3-hIgG1-L6-hIL-2 (K43E/D20A) | 151 | 13 | 2 |
| 1H3-hIgG1-L6-hIL-2 (E61A/D20A) | 152 | 14 | 2 |
| 1H3-hIgG1-L6-hIL-2 (E62A/D20A) | 153 | 14 | 2 |
| 1H3-hIgG1-L6-hIL-2 (E62Y/D20A) | 154 | 14 | 3 |
| 1H3-hIgG1-L6-hIL-2 (L72D/D20A) | 155 | 14 | 2 |
| 1H3-hIgG1-L6-hIL-2 (L72H/D20A) | 156 | 14 | 3 |
| 1H3-hIgG1-L6-hIL-2 (L72R/D20A) | 157 | 10 | 3 |
| 1H3-hIgG1-L6-hIL-2 (F42D/I92D) | 158 | 12 | 5 |
| 1H3-hIgG1-L6-hIL-2 (F42R/I92D) | 159 | 12 | 3 |
| 1H3-hIgG1-L6-hIL-2 (F42H/I92D) | 160 | 12 | 2 |
| 1H3-hIgG1-L6-hIL-2 (F42A/I92D) | 161 | 12 | 3 |
| 1H3-hIgG1-L6-hIL-2 (K43E/I92D) | 162 | 13 | 4 |
| 1H3-hIgG1-L6-hIL-2 (Y45R/I92D) | 163 | 13 | 1 |
| 1H3-hIgG1-L6-hIL-2 (Y45K/I92D) | 164 | 13 | 1 |
| 1H3-hIgG1-L6-hIL-2 (E62A/I92D) | 165 | 13 | 3 |
| 1H3-hIgG1-L6-hIL-2 (E62Y/I92D) | 166 | 14 | 5 |
| 1H3-hIgG1-L6-hIL-2 (L72D/I92D) | 167 | 14 | 5 |
| 1H3-hIgG1-L6-hIL-2 (L72H/I92D) | 168 | 14 | 5 |
| 1H3-hIgG1-L6-hIL-2 (L72R/I92D) | 169 | 14 | 5 |
| 1H3-hIgG1-L6-hIL-2 (R38D/I92D) | 170 | 15 | 2 |
| 1H3-hIgG1-L6-hIL-2 (R38E/I92D) | 171 | 15 | 2 |
| 1H3-hIgG1-L6-hIL-2 (R38A/I92D) | 172 | 14 | 2 |
| 1H3-hIgG1-L6-hIL-2 (R38Q/I92D) | 173 | 13 | 4 |
| 1H3-hIgG1-L6-hIL-2 (R38E/N88R) | 174 | 16 | 1 |
| 1H3-hIgG1-L6-hIL-2 (R38E/D84R) | 175 | 14 | 2 |

TABLE 7-continued

| Fold change from rhIL-2 in a fixed concentration pSTAT5 screen on 1H3-hlgG1-L6-hIL-2 fusion proteins from Group 5 | | | |
|--|-------------------------------------|---|--|
| Variants | SEQ ID NO of hIL-2 variant | Fold change from hIL-2 (NK-92) | Fold change from hIL-2 (TF1 + IL-2Rβ) |
| 1H3-hlgG1-L6-hIL-2 (R38E/D84K) | 176 | 14 | 2 |
| 1H3-hlgG1-L6-hIL-2 (F42A/Y45R/D20A) | 177 | 11 | 2 |
| 1H3-hlgG1-L6-hIL-2 (F42H/Y45R/D20A) | 178 | 12 | 2 |
| 1H3-hlgG1-L6-hIL-2 (R38D/E61R/D20A) | 179 | 12 | 3 |
| 1H3-hlgG1-L6-hIL-2 (R38E/E61R/D20A) | 180 | 11 | 3 |
| 1H3-hlgG1-L6-hIL-2 (R38Q/E61R/D20A) | 181 | 12 | 3 |
| 1H3-hlgG1-L6-hIL-2 (R38A/E61R/D20A) | 182 | 13 | 3 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/R38A) | 183 | 6 | 5 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/R38D) | 184 | 21 | 6 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/R38E) | 185 | 21 | 5 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/R38Q) | 186 | 19 | 6 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/F42R) | 187 | 21 | 4 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/F42A) | 188 | 21 | 5 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/F42D) | 189 | 22 | 12 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/F42H) | 190 | 22 | 4 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/F42K) | 191 | 21 | 4 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/K43A) | 192 | 5 | 7 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/K43E) | 193 | 13 | 6 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/K43Q) | 194 | 5 | 6 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/Y45A) | 195 | 4 | 5 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/Y45K) | 196 | 22 | 6 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/Y45S) | 197 | 5 | 6 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/Y45R) | 198 | 25 | 6 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/E61A) | 199 | 10 | 6 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/E62A) | 200 | 23 | 6 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/E62R) | 201 | 25 | 17 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/E62K) | 202 | 25 | 15 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/E62Y) | 203 | 25 | 10 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/E68Y) | 204 | 8 | 5 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/E68A) | 205 | 5 | 8 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/E68L) | 206 | 7 | 9 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/L72Y) | 207 | 1 | 5 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/L72R) | 208 | 12 | 9 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/L72A) | 209 | 2 | 6 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/L72D) | 210 | 21 | 6 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/L72H) | 211 | 14 | 6 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/L72F) | 212 | 2 | 6 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/F42K/Y45R) | 214 | 21 | 5 |
| 1H3-hlgG1-L6-hIL-2 (D20A/R38E/C125A) | 215 | 16 | 3 |
| 1H3-hlgG1-L6-hIL-2 (T3A/D20A/R38E) | 216 | 18 | 2 |
| 1H3-hlgG1-L6-hIL-2 (T3A/D20A/R38E/C125A) | 217 | 18 | 3 |
| 1H3-hlgG1-L6-hIL-2 (A1-3APT/D20A/R38E) | 218 | 13 | 1 |
| 1H3-hlgG1-L6-hIL-2 (A1-3APT/D20A/R38E/C125A) | 219 | 15 | 4 |
| 1H3-hlgG1-L6-hIL-2 (R38E/Q22A) | 220 | 12 | 0 |
| 1H3-hlgG1-L6-hIL-2 (R38E/T123A) | 221 | 12 | 0 |
| 1H3-hlgG1-L6-hIL-2 (R38E/I129A) | 222 | 13 | 1 |
| 1H3-hlgG1-L6-hIL-2 (R38E/S130A) | 223 | 12 | 0 |
| 1H3-hlgG1-L6-hIL-2 (R38E/Q126A) | 224 | 13 | 1 |
| 1H3-hlgG1-L6-hIL-2 (R38E/Q126D) | 225 | 15 | 4 |
| 1H3-hlgG1-L6-hIL-2 (R38E/Q126V) | 226 | 14 | 1 |
| 1H3-hlgG1-L6-hIL-2 (R38E/Q22A/S130A) | 227 | 13 | 1 |

TABLE 8

| Fold change from rhIL-2 in a fixed concentration pSTAT5 screen on 1H3-hlgG1-L6-hIL-2 fusion proteins from Group 6 | | | |
|--|-------------------------------------|--------------------------------------|--|
| Variants | SEQ ID NO of hIL-2 variant | Fold change from hIL-2 (NK-92) | Fold change from hIL-2 (TF1 + IL-2Rβ) |
| 1H3-hlgG1-L6-hIL-2 (D20A/E61R) | 230 | 25 | 4 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E61N) | 231 | 15 | 1 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E61D) | 232 | 11 | 0 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E61Q) | 233 | 16 | 2 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E61G) | 234 | 15 | 2 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E61H) | 235 | 15 | 2 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E61I) | 236 | 16 | 1 |

TABLE 8-continued

| Fold change from rhIL-2 in a fixed concentration pSTAT5 screen on 1H3-hlgG1-L6-hIL-2 fusion proteins from Group 6 | | | |
|--|-------------------------------------|--------------------------------------|--|
| Variants | SEQ ID NO of hIL-2 variant | Fold change from hIL-2 (NK-92) | Fold change from hIL-2 (TF1 + IL-2Rβ) |
| 1H3-hlgG1-L6-hIL-2 (D20A/E61L) | 237 | 16 | 1 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E61K) | 238 | 17 | 2 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E61M) | 239 | 15 | 2 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E61F) | 240 | 14 | 0 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E61P) | 241 | 15 | 1 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E61S) | 242 | 16 | 1 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E61T) | 243 | 16 | 2 |

TABLE 8-continued

| Fold change from rhIL-2 in a fixed concentration pSTAT5 screen on 1H3-hlgG1-L6-hIL-2 fusion proteins from Group 6 | | | |
|---|----------------------------|--------------------------------|--|
| Variants | SEQ ID NO of hIL-2 variant | Fold change from hIL-2 (NK-92) | Fold change from hIL-2 (TF1 + IL-2Rβ) ⁵ |
| 1H3-hlgG1-L6-hIL-2 (D20A/E61W) | 244 | 15 | 2 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E61Y) | 245 | 15 | 2 |
| 1H3-hlgG1-L6-hIL-2 (D20A/E61V) | 246 | 17 | 3 |
| 1H3-hlgG1-L6-hIL-2 (D20A/F42N) | 247 | 15 | 2 |
| 1H3-hlgG1-L6-hIL-2 (D20A/F42Q) | 248 | 15 | 2 |
| 1H3-hlgG1-L6-hIL-2 (D20A/F42E) | 249 | 16 | 1 |
| 1H3-hlgG1-L6-hIL-2 (D20A/F42G) | 250 | 17 | 2 |
| 1H3-hlgG1-L6-hIL-2 (D20A/F42I) | 251 | 17 | 2 |
| 1H3-hlgG1-L6-hIL-2 (D20A/F42L) | 252 | 14 | 2 |
| 1H3-hlgG1-L6-hIL-2 (D20A/F42M) | 253 | 15 | 2 |
| 1H3-hlgG1-L6-hIL-2 (D20A/F42P) | 254 | 17 | 2 |
| 1H3-hlgG1-L6-hIL-2 (D20A/F42S) | 255 | 15 | 2 |
| 1H3-hlgG1-L6-hIL-2 (D20A/F42T) | 256 | 16 | 2 |
| 1H3-hlgG1-L6-hIL-2 (D20A/F42W) | 257 | 16 | 2 |
| 1H3-hlgG1-L6-hIL-2 (D20A/F42Y) | 258 | 17 | 2 |
| 1H3-hlgG1-L6-hIL-2 (D20A/F42V) | 259 | 18 | 2 |
| 1H3-hlgG1-L6-hIL-2 (D20A/Y45A) | 260 | 15 | 2 |
| 1H3-hlgG1-L6-hIL-2 (D20A/Y45N) | 261 | 14 | 2 |
| 1H3-hlgG1-L6-hIL-2 (D20A/Y45D) | 262 | 18 | 3 |
| 1H3-hlgG1-L6-hIL-2 (D20A/Y45Q) | 263 | 17 | 3 |
| 1H3-hlgG1-L6-hIL-2 (D20A/Y45E) | 264 | 18 | 3 |
| 1H3-hlgG1-L6-hIL-2 (D20A/Y45G) | 265 | 18 | 2 |
| 1H3-hlgG1-L6-hIL-2 (D20A/Y45H) | 266 | 16 | 2 |
| 1H3-hlgG1-L6-hIL-2 (D20A/Y45I) | 267 | 13 | 2 |
| 1H3-hlgG1-L6-hIL-2 (D20A/Y45L) | 268 | 13 | 2 |
| 1H3-hlgG1-L6-hIL-2 (D20A/Y45M) | 269 | 16 | 3 |
| 1H3-hlgG1-L6-hIL-2 (D20A/Y45F) | 270 | 13 | 2 |
| 1H3-hlgG1-L6-hIL-2 (D20A/Y45P) | 271 | 25 | 4 |
| 1H3-hlgG1-L6-hIL-2 (D20A/Y45S) | 272 | 14 | 3 |
| 1H3-hlgG1-L6-hIL-2 (D20A/Y45T) | 273 | 24 | 3 |
| 1H3-hlgG1-L6-hIL-2 (D20A/Y45W) | 274 | 19 | 3 |
| 1H3-hlgG1-L6-hIL-2 (D20A/Y45V) | 275 | 21 | 3 |
| 1H3-hlgG1-L6-hIL-2 (I92D/F42N) | 276 | 29 | 5 |
| 1H3-hlgG1-L6-hIL-2 (I92D/F42Q) | 277 | 29 | 4 |
| 1H3-hlgG1-L6-hIL-2 (I92D/F42E) | 278 | 30 | 5 |
| 1H3-hlgG1-L6-hIL-2 (I92D/F42G) | 279 | 32 | 5 |
| 1H3-hlgG1-L6-hIL-2 (I92D/F42I) | 280 | 31 | 4 |
| 1H3-hlgG1-L6-hIL-2 (I92D/F42L) | 281 | 31 | 5 |
| 1H3-hlgG1-L6-hIL-2 (I92D/F42K) | 282 | 26 | 4 |
| 1H3-hlgG1-L6-hIL-2 (I92D/F42M) | 283 | 28 | 5 |
| 1H3-hlgG1-L6-hIL-2 (I92D/F42P) | 284 | 29 | 4 |
| 1H3-hlgG1-L6-hIL-2 (I92D/F42S) | 285 | 30 | 5 |
| 1H3-hlgG1-L6-hIL-2 (I92D/F42T) | 286 | 28 | 3 |
| 1H3-hlgG1-L6-hIL-2 (I92D/F42W) | 287 | 18 | 4 |
| 1H3-hlgG1-L6-hIL-2 (I92D/F42Y) | 288 | 22 | 3 |
| 1H3-hlgG1-L6-hIL-2 (I92D/F42V) | 289 | 30 | 3 |
| 1H3-hlgG1-L6-hIL-2 (I92D/Y45A) | 290 | 11 | 3 |
| 1H3-hlgG1-L6-hIL-2 (I92D/Y45N) | 291 | 4 | 3 |
| 1H3-hlgG1-L6-hIL-2 (I92D/Y45D) | 292 | 29 | 5 |
| 1H3-hlgG1-L6-hIL-2 (I92D/Y45Q) | 293 | 25 | 3 |
| 1H3-hlgG1-L6-hIL-2 (I92D/Y45E) | 294 | 27 | 4 |
| 1H3-hlgG1-L6-hIL-2 (I92D/Y45G) | 295 | 20 | 3 |
| 1H3-hlgG1-L6-hIL-2 (I92D/Y45H) | 296 | 7 | 3 |
| 1H3-hlgG1-L6-hIL-2 (I92D/Y45I) | 297 | 20 | 4 |
| 1H3-hlgG1-L6-hIL-2 (I92D/Y45L) | 298 | 5 | 3 |
| 1H3-hlgG1-L6-hIL-2 (I92D/Y45M) | 299 | 14 | 3 |
| 1H3-hlgG1-L6-hIL-2 (I92D/Y45F) | 300 | 10 | 3 |
| 1H3-hlgG1-L6-hIL-2 (I92D/Y45P) | 301 | 28 | 4 |
| 1H3-hlgG1-L6-hIL-2 (I92D/Y45S) | 302 | 11 | 3 |
| 1H3-hlgG1-L6-hIL-2 (I92D/Y45T) | 303 | 28 | 4 |
| 1H3-hlgG1-L6-hIL-2 (I92D/Y45W) | 304 | 27 | 4 |
| 1H3-hlgG1-L6-hIL-2 (I92D/Y45V) | 305 | 28 | 5 |
| 1H3-hlgG1-L6-hIL-2 (R38E/D20H) | 306 | 17 | 5 |
| 1H3-hlgG1-L6-hIL-2 (R38E/D20S) | 307 | 17 | 3 |
| 1H3-hlgG1-L6-hIL-2 (F42A/N88R) | 308 | 18 | 3 |
| 1H3-hlgG1-L6-hIL-2 (F42A/N88D) | 309 | 18 | 3 |
| 1H3-hlgG1-L6-hIL-2 (R38E/D84A) | 310 | 18 | 1 |
| 1H3-hlgG1-L6-hIL-2 (R38E/D84N) | 311 | 18 | 1 |
| 1H3-hlgG1-L6-hIL-2 (R38E/D84Q) | 312 | 18 | 1 |
| 1H3-hlgG1-L6-hIL-2 (R38E/D84E) | 313 | 16 | 1 |
| 1H3-hlgG1-L6-hIL-2 (R38E/D84G) | 314 | 18 | 1 |
| 1H3-hlgG1-L6-hIL-2 (R38E/D84H) | 315 | 19 | 2 |

TABLE 8-continued

| Fold change from rhIL-2 in a fixed concentration pSTAT5 screen on 1H3-hlgG1-L6-hIL-2 fusion proteins from Group 6 | | | |
|---|----------------------------|--------------------------------|---------------------------------------|
| Variants | SEQ ID NO of hIL-2 variant | Fold change from hIL-2 (NK-92) | Fold change from hIL-2 (TF1 + IL-2Rβ) |
| 1H3-hlgG1-L6-hIL-2 (R38E/D84I) | 316 | 20 | 1 |
| 1H3-hlgG1-L6-hIL-2 (R38E/D84L) | 317 | 19 | 1 |
| 1H3-hlgG1-L6-hIL-2 (R38E/D84M) | 318 | 20 | 2 |
| 1H3-hlgG1-L6-hIL-2 (R38E/D84F) | 319 | 20 | 2 |
| 1H3-hlgG1-L6-hIL-2 (R38E/D84P) | 320 | 20 | 1 |
| 1H3-hlgG1-L6-hIL-2 (R38E/D84S) | 321 | 21 | 1 |
| 1H3-hlgG1-L6-hIL-2 (R38E/D84T) | 322 | 20 | 1 |
| 1H3-hlgG1-L6-hIL-2 (R38E/D84W) | 323 | 21 | 1 |
| 1H3-hlgG1-L6-hIL-2 (R38E/D84Y) | 324 | 21 | 1 |
| 1H3-hlgG1-L6-hIL-2 (R38E/D84V) | 325 | 22 | 1 |
| 1H3-hlgG1-L6-hIL-2 (R38E/I92A) | 326 | 22 | 1 |
| 1H3-hlgG1-L6-hIL-2 (R38E/I92R) | 327 | 22 | 2 |
| 1H3-hlgG1-L6-hIL-2 (R38E/I92N) | 328 | 22 | 1 |
| 1H3-hlgG1-L6-hIL-2 (R38E/I92Q) | 329 | 22 | 1 |
| 1H3-hlgG1-L6-hIL-2 (R38E/I92E) | 330 | 22 | 2 |
| 1H3-hlgG1-L6-hIL-2 (R38E/I92G) | 331 | 22 | 1 |
| 1H3-hlgG1-L6-hIL-2 (R38E/I92H) | 332 | 21 | 1 |
| 1H3-hlgG1-L6-hIL-2 (R38E/I92L) | 333 | 17 | 1 |
| 1H3-hlgG1-L6-hIL-2 (R38E/I92K) | 334 | 24 | 3 |
| 1H3-hlgG1-L6-hIL-2 (R38E/I92M) | 335 | 20 | 1 |
| 1H3-hlgG1-L6-hIL-2 (R38E/I92F) | 336 | 16 | 1 |
| 1H3-hlgG1-L6-hIL-2 (R38E/I92P) | 337 | 24 | 5 |
| 1H3-hlgG1-L6-hIL-2 (R38E/I92S) | 338 | 22 | 2 |
| 1H3-hlgG1-L6-hIL-2 (R38E/I92T) | 339 | 22 | 1 |
| 1H3-hlgG1-L6-hIL-2 (R38E/I92W) | 340 | 23 | 1 |
| 1H3-hlgG1-L6-hIL-2 (R38E/I92Y) | 341 | 21 | 1 |
| 1H3-hlgG1-L6-hIL-2 (R38E/I92V) | 342 | 21 | 1 |
| 1H3-hlgG1-L6-hIL-2 (R38E/H16E) | 343 | 25 | 3 |
| 1H3-hlgG1-L6-hIL-2 (R38K/D20A) | 344 | 17 | 3 |

Example 4: Testing for Attenuation of IL-2 Fusion Proteins for Each of the High-Affinity and Intermediate-Affinity hIL-2 Receptors with a Cell-Based Potency pSTAT5 Dose-Titration Screen

40 The attenuation of selected antibody-attenuated hIL-2 fusion proteins described in Example 2 (1H3-hlgG1-L6-hIL-2 fusion protein from Groups 2-6) were tested in pSTAT5 titration curves using the NK-92 and TF1+IL-2Rβ cell lines as described in Protocol D.

45 The gMFI of the Alexa Fluor 647 pSTAT5-positive signal was used to generate four parameter logistic curves and GraphPad Prism 7 software was then used to calculate EC₅₀ values. These values were compared to recombinant hIL-2 (rhIL-2) control as a measurement of attenuation. Tables 50 9-13 summarize the fold change in activity from rhIL-2 calculated using the gMFI of the Alexa Fluor 647 signal.

An increase in the fold change from rhIL-2 was indicative of the degree of attenuation of hIL-2 activity. Each antibody-attenuated hIL-2 fusion protein tested in the pSTAT5 titration curve was also assessed for agonistic activity and characterized as either full, partial, or no activity (inactive). Antibody-attenuated hIL-2 fusion protein dose-titration curves that reached the maximal gMFI level as the rhIL-2 were considered to be variants with full agonist activity. 60 Partial agonist activity was calculated as described in Example 3. Inactive antibody-attenuated hIL-2 fusion proteins were classified as having less than 10% activity in comparison to rhIL-2. Some fold changes from rhIL-2 could not be accurately calculated (denoted as Not Calculated or 65 “NC”) using the GraphPad Prism 7 software since a full four parameter logistic curve was not generated and accordingly these values are an estimate (annotated as ^a in Tables 9-13).

However, these variants had greater than 10,000-fold attenuation from rhIL-2 on graphs (data not shown). This is denoted on Tables 9-13 as “>10,000 on graph; NC”

Full titration pSTAT5 curves demonstrated similar findings as presented in Example 3 in which substitutions that modulated binding to both the alpha chain and the beta chain substantially attenuated IL-2 activity on the high affinity

IL-2 receptor in comparison to single substitutions for binding to the alpha or beta chain only. The full titration pSTAT5 assay was additionally able to differentiate between variants with substitutions that caused inactivity versus highly attenuated variants. Finally, comparison of dose-titration curves illustrated more accurate of levels of attenuation over a fixed concentration assay.

TABLE 9

| Fold change from rhIL-2 and agonistic activity on 1H3-hIgG1-L6-hIL-2 fusion proteins from Group 2 | | | | | |
|---|----------------------------|---------------------------------|----------------------------|--|-----------------------------------|
| Variants | SEQ ID NO of hIL-2 variant | Fold change from rhIL-2 (NK-92) | Agonistic Activity (NK-92) | Fold change from rhIL-2 (TF1 + IL-2Rβ) | Agonistic Activity (TF1 + IL-2Rβ) |
| 1H3-hIgG1-L6-hIL-2 (R38A) | 46 | 2 | Full | 0 | Full |
| 1H3-hIgG1-L6-hIL-2 (R38D) | 47 | 55 | Full | 1 | Full |
| 1H3-hIgG1-L6-hIL-2 (R38E) | 48 | 99-136 | Full | 0 | Full |
| 1H3-hIgG1-L6-hIL-2 (F42R) | 50 | 65 | Full | 0 | Full |
| 1H3-hIgG1-L6-hIL-2 (F42D) | 52 | 193 | Full | 0 | Full |
| 1H3-hIgG1-L6-hIL-2 (K43A) | 54 | 3 ^a | Full | 0 | Full |
| 1H3-hIgG1-L6-hIL-2 (Y45R) | 57 | 81 ^a | Full | 0 | Full |
| 1H3-hIgG1-L6-hIL-2 (E61A) | 61 | 3 ^a | Full | 0 | Full |
| 1H3-hIgG1-L6-hIL-2 (E61R) | 62 | 22 ^a | Full | 0 | Full |
| 1H3-hIgG1-L6-hIL-2 (E61K) | 63 | 14 ^a | Full | 0 | Full |
| 1H3-hIgG1-L6-hIL-2 (E62A) | 64 | 6 ^a | Full | 0 | Full |
| 1H3-hIgG1-L6-hIL-2 (E62R) | 65 | >10,000 | Partial, 80% | 38 | Full |
| 1H3-hIgG1-L6-hIL-2 (E62K) | 66 | 2048 | Full | 10 | Full |
| 1H3-hIgG1-L6-hIL-2 (E62Y) | 67 | 18 | Full | 0 | Full |
| 1H3-hIgG1-L6-hIL-2 (E68K) | 70 | 2 ^a | Full | 0 | Full |
| 1H3-hIgG1-L6-hIL-2 (E68R) | 71 | 3 ^a | Full | 0 | Full |
| 1H3-hIgG1-L6-hIL-2 (L72R) | 74 | 2 ^a | Full | 1 | Full |
| 1H3-hIgG1-L6-hIL-2 (L72D) | 76 | 4 ^a | Full | 0 | Full |
| 1H3-hIgG1-L6-hIL-2 (L72H) | 77 | 1 ^a | Partial, 80% | 0 | Full |
| 1H3-hIgG1-L6-hIL-2 (R38D/E61R) | 79 | 479 | Partial, 80% | NT | NT |
| 1H3-hIgG1-L6-hIL-2 (R38D/E61R/K43E) | 80 | 598 | Full | NT | NT |
| 1H3-hIgG1-L6-hIL-2 (T3A/F42A/Y45A/L72G/C125A) | 81 | 360-1426 | Full | 0 | Full |

NT = not tested

^a = Fold change is an estimate only since a full four parameter logistic curve was not reached

TABLE 10

| Fold change from rhIL-2 and agonistic activity on 1H3-hIgG1-L6-hIL-2 fusion proteins variants from Group 3 | | | | | |
|--|----------------------------|---------------------------------|----------------------------|--|-----------------------------------|
| Variants | SEQ ID NO of hIL-2 variant | Fold change from rhIL-2 (NK-92) | Agonistic Activity (NK-92) | Fold change from rhIL-2 (TF1 + IL-2Rβ) | Agonistic Activity (TF1 + IL-2Rβ) |
| 1H3-hIgG1-L6-hIL-2 (H16E) | 87 | 63 | Full | 63 | Full |
| 1H3-hIgG1-L6-hIL-2 (L19A) | 88 | 0 | Full | 0 | Full |
| 1H3-hIgG1-L6-hIL-2 (D20I) | 89 | NT | NT | >10,000 on graph, NC ^a | Inactive |
| 1H3-hIgG1-L6-hIL-2 (D20S) | 90 | 28 | Partial, 80% | 277 ^a | Partial, 80% |
| 1H3-hIgG1-L6-hIL-2 (D20H) | 91 | >10,000 ^a | Partial, 90% | 2767 ^a | Partial, 50% |
| 1H3-hIgG1-L6-hIL-2 (D20W) | 93 | NT | NT | >10,000 on graph, NC ^a | Inactive |
| 1H3-hIgG1-L6-hIL-2 (D20Y) | 94 | >10,000 ^a | Partial, 50-70% | 84-143 ^a | Partial, 80% |
| 1H3-hIgG1-L6-hIL-2 (D20R) | 95 | NT | NT | >10,000 on graph, NC ^a | Inactive |
| 1H3-hIgG1-L6-hIL-2 (D20F) | 96 | NT | NT | >10,000 on graph, NC ^a | Inactive |
| 1H3-hIgG1-L6-hIL-2 (D84A) | 98 | NT | NT | 14 | Full |
| 1H3-hIgG1-L6-hIL-2 (D84R) | 99 | 16 | Full | 244 ^a | Partial, 70% |
| 1H3-hIgG1-L6-hIL-2 (D84K) | 100 | 14 | Partial, 90% | 195 ^a | Full |
| 1H3-hIgG1-L6-hIL-2 (N88Y) | 102 | NT | NT | >10,000 on graph, NC ^a | Inactive |

TABLE 10-continued

| Fold change from rhIL-2 and agonistic activity on 1H3-hIgG1-L6-hIL-2 fusion proteins variants from Group 3 | | | | | |
|--|----------------------------|---------------------------------|----------------------------|--|-----------------------------------|
| Variants | SEQ ID NO of hIL-2 variant | Fold change from rhIL-2 (NK-92) | Agonistic Activity (NK-92) | Fold change from rhIL-2 (TF1 + IL-2Rβ) | Agonistic Activity (TF1 + IL-2Rβ) |
| 1H3-hIgG1-L6-hIL-2 (N88D) | 103 | 21 | Partial, 90% | 130 | Full |
| 1H3-hIgG1-L6-hIL-2 (N88R) | 104 | 5-27 | Partial, 80%-Full | 289-556 | Partial, 40% |
| 1H3-hIgG1-L6-hIL-2 (N88E) | 105 | NT | NT | >10,000 on graph, NC ^a | Partial, 40% |
| 1H3-hIgG1-L6-hIL-2 (N88F) | 106 | NT | NT | >10,000 on graph, NC ^a | Inactive |
| 1H3-hIgG1-L6-hIL-2 (N88I) | 107 | NT | NT | >10,000 on graph, NC ^a | Inactive |
| 1H3-hIgG1-L6-hIL-2 (I92Y) | 109 | NT | NT | 1 | Full |
| 1H3-hIgG1-L6-hIL-2 (I92S) | 110 | NT | NT | 8 | Full |
| 1H3-hIgG1-L6-hIL-2 (I92R) | 112 | NT | NT | 31 | Full |
| 1H3-hIgG1-L6-hIL-2 (I92D) | 113 | 8-20 | Full | 68-365 ^a | Partial, 70-90% |
| 1H3-hIgG1-L6-hIL-2 (E95R) | 116 | NT | NT | 5 | Full |
| 1H3-hIgG1-L6-hIL-2 (D20T) | 92 | 8 | Full | 167 ^a | Partial, 80% |
| 1H3-hIgG1-L6-hIL-2 (D20A) | 31 | 21 | Partial, 80% | 117 ^a | Partial, 80% |
| 1H3-hIgG1-L6-hIL-2 (D20Y/H16E) | 94 | 52 ^a | Partial, 80% | 2159 ^a | Partial, 30% |
| 1H3-hIgG1-L6-hIL-2 (D20Y/H16A) | 119 | >10,000 ^a | Partial, 40% | 30 ^a | Partial, 20% |
| 1H3-hIgG1-L6-hIL-2 (D20Y/H16Y) | 120 | >10,000 ^a | Partial, 40% | 343 ^a | Partial, 20% |
| 1H3-hIgG1-L6-hIL-2 (D20Y/I92A) | 121 | >10,000 ^a | Partial, 20% | 4 ^a | Partial, 10% |
| 1H3-hIgG1-L6-hIL-2 (D20Y/I92S) | 122 | >10,000 ^a | Partial, 10% | 12 ^a | Partial, 10% |

NT = Not Tested; NC = Not Calculated by GraphPad Prism 7

^a = Fold change is an estimate only since a full four parameter logistic curve was not reached

TABLE 11

| Fold change from rhIL-2 and agonistic activity on 1H3-hIgG1-L6-hIL-2 fusion proteins from Group 4 | | | | | | |
|---|----------------------------|---------------------------------|----------------------------|--|-----------------------------------|--|
| Variants | SEQ ID NO of hIL-2 variant | Fold change from rhIL-2 (NK-92) | Agonistic Activity (NK-92) | Fold change from rhIL-2 (TF1 + IL-2Rβ) | Agonistic Activity (TF1 + IL-2Rβ) | |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (E15A) | 82 | 184 | Full | 20 | Full | |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (D20I) | 89 | >10,000 ^a | Partial, 80% | >10,000 on graph, NC ^a | Inactive | |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (D20S) | 90 | 2403 | Full | >10,000 on graph, NC ^a | Inactive | |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (D20H) | 91 | >10,000 ^a | Partial, 80% | >10,000 on graph, NC ^a | Inactive | |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (D20W) | 93 | >10,000 ^a | Partial, 60% | >10,000 on graph, NC ^a | Inactive | |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (D20Y) | 94 | >10,000 ^a | Partial, 90% | >10,000 on graph, NC ^a | Inactive | |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (D20R) | 95 | >10,000 ^a | Partial, 80% | >10,000 on graph, NC ^a | Inactive | |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (D20F) | 96 | >10,000 ^a | Partial, 70% | >10,000 on graph, NC ^a | Inactive | |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (D84K) | 100 | >10,000 | Full | >10,000 on graph, NC ^a | Inactive | |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (S87A) | 101 | 305 | Full | 44 | Full | |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (N88Y) | 102 | >10,000 ^a | Partial, 50% | >10,000 on graph, NC ^a | Inactive | |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (N88D) | 103 | 393 | Full | >10,000 on graph, NC ^a | Inactive | |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (N88R) | 104 | 274 | Full | >10,000 on graph, NC ^a | Inactive | |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (N88E) | 105 | >10,000 ^a | Full | >10,000 on graph, NC ^a | Inactive | |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (N88F) | 106 | >10,000 ^a | Partial, 80% | >10,000 on graph, NC ^a | Inactive | |

TABLE 11-continued

| Fold change from rhIL-2 and agonistic activity on 1H3-hIgG1-L6-hIL-2 fusion proteins from Group 4 | | | | | |
|---|---------------------|---------------------------------|----------------------------|--|-----------------------------------|
| Variants | SEQ ID | | Agonistic Activity (NK-92) | Fold change from rhIL-2 (TF1 + IL-2Rβ) | Agonistic Activity (TF1 + IL-2Rβ) |
| | NO of hIL-2 variant | Fold change from rhIL-2 (NK-92) | | | |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (N88I) | 107 | 7780 | Full | >10,000 on graph, NC ^a | Inactive |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (I92A) | 108 | 26 | Full | 95 | Full |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (E95A) | 115 | 30 | Full | 16 | Full |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (E95K) | 117 | 792 | Full | 434 ^a | Partial, 60% |

NC = Not Calculated by GraphPad Prism 7

^a = Fold change is an estimate only since a full four parameter logistic curve was not reached

TABLE 12

| Fold change from rhIL-2 and agonistic activity on 1H3-hIgG1-L6-hIL-2 fusion proteins from Group 5 | | | | | |
|---|---------------------|-----------------------------------|----------------------------|--|-----------------------------------|
| Variants | SEQ ID | | Agonistic Activity (NK-92) | Fold change from rhIL-2 (TF1 + IL-2Rβ) | Agonistic Activity (TF1 + IL-2Rβ) |
| | NO of hIL-2 variant | Fold change from rhIL-2 (NK-92) | | | |
| 1H3-hIgG1-L6-hIL-2 (F42K/D20A) | 129 | >10,000 ^a | Partial, 30% | 219 ^a | Partial, 50% |
| 1H3-hIgG1-L6-hIL-2 (F42A/D20A) | 130 | >10,000 ^a | Partial, 70% | 96 ^a | Partial, 70% |
| 1H3-hIgG1-L6-hIL-2 (R38N/D20A) | 134 | 4497 | Partial, 70% | 121 ^a | Partial, 70% |
| 1H3-hIgG1-L6-hIL-2 (R38G/D20A) | 135 | 2811 | Partial, 70% | 139 ^a | Partial, 70% |
| 1H3-hIgG1-L6-hIL-2 (R38H/D20A) | 136 | 1752 | Partial, 80% | 107 ^a | Partial, 70% |
| 1H3-hIgG1-L6-hIL-2 (R38I/D20A) | 137 | 658 | Partial, 70% | 107 ^a | Partial, 60% |
| 1H3-hIgG1-L6-hIL-2 (R38L/D20A) | 138 | 532 | Partial, 80% | 125 ^a | Partial, 70% |
| 1H3-hIgG1-L6-hIL-2 (R38M/D20A) | 139 | 786 | Partial, 90% | 85 ^a | Partial, 90% |
| 1H3-hIgG1-L6-hIL-2 (R38F/D20A) | 140 | 1072 | Partial, 80% | 124 ^a | Partial, 90% |
| 1H3-hIgG1-L6-hIL-2 (R38P/D20A) | 142 | 337 | Partial, 70% | 337 ^a | Partial, 80% |
| 1H3-hIgG1-L6-hIL-2 (R38S/D20A) | 142 | 571 | Partial, 70% | 571 ^a | Partial, 90% |
| 1H3-hIgG1-L6-hIL-2 (R38V/D20A) | 146 | 765 | Partial, 70% | 765 ^a | Partial, 90% |
| 1H3-hIgG1-L6-hIL-2 (R38A/D20A) | 147 | 619 | Partial, 80% | 70 ^a | Partial, 70% |
| 1H3-hIgG1-L6-hIL-2 (R38Q/D20A) | 148 | 4700 | Partial, 80% | 91 ^a | Partial, 70% |
| 1H3-hIgG1-L6-hIL-2 (D20A/R38E) | 149 | >10,000 ^a | Partial, 60%-Full | 409 ^a | Partial, 50% |
| 1H3-hIgG1-L6-hIL-2 (R38D/D20A) | 150 | >10,000 ^a | Partial, 70% | 172 ^a | Partial, 70% |
| 1H3-hIgG1-L6-hIL-2 (K43E/D20A) | 151 | 584 | Partial, 90% | 231 ^a | Partial, 70% |
| 1H3-hIgG1-L6-hIL-2 (F42R/I92D) | 159 | 801 ^a | Partial, 40% | 52 ^a | Partial, 80% |
| 1H3-hIgG1-L6-hIL-2 (F42H/I92D) | 160 | 194 | Full | 801 ^a | Partial, 80% |
| 1H3-hIgG1-L6-hIL-2 (F42A/I92D) | 161 | 338 ^a | Partial, 70% | 194 ^a | Full |
| 1H3-hIgG1-L6-hIL-2 (R38D/I92D) | 170 | >10,000 ^a | Partial, 80% | 338 ^a | Partial, 80% |
| 1H3-hIgG1-L6-hIL-2 (R38E/I92D) | 171 | >10,000 ^a | Partial, 70% | 51 ^a | Partial, 80% |
| 1H3-hIgG1-L6-hIL-2 (R38Q/I92D) | 172 | 561 | Full | 48 ^a | Partial, 90% |
| 1H3-hIgG1-L6-hIL-2 (R38E/D84R) | 175 | >10,000 ^a | Partial, 60% | 50 ^a | Partial, 80% |
| 1H3-hIgG1-L6-hIL-2 (R38E/D84K) | 176 | >10,000 ^a | Partial, 40% | 45 ^a | Partial, 80% |
| 1H3-hIgG1-L6-hIL-2 (R38D/E61R/D20A) | 179 | >10,000 on graph, NC ^a | Partial, 40% | 62 ^a | Partial, 70% |
| 1H3-hIgG1-L6-hIL-2 (R38E/E61R/D20A) | 180 | >10,000 ^a | Partial, 90% | 181 ^a | Partial, 60% |
| 1H3-hIgG1-L6-hIL-2 (R38Q/E61R/D20A) | 181 | >10,000 ^a | Partial, 40% | 115 ^a | Partial, 80% |
| 1H3-hIgG1-L6-hIL-2 (R38A/E61R/D20A) | 182 | >10,000 ^a | Partial, 40% | 130 ^a | Partial, 60% |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/R38A) | 183 | 149-199 | Partial, 70-80% | 157 ^a | Partial, 70% |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/R38D) | 184 | >10,000 | Partial, 60-70% | 84-508 ^a | Full |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/R38E) | 185 | >10,000 ^a | Partial, 70-90% | 188-427 ^a | Partial, 70%-Full |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/R38Q) | 186 | 3725 | Partial, 70% | 124-413 ^a | Partial, 80%-Full |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/F42R) | 187 | >10,000 ^a | Partial, 70% | 87 ^a | Partial, 60% |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/F42A) | 188 | 3000-5718 ^a | Partial, 90% | 45-244 ^a | Partial, 70%-Full |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/F42D) | 189 | >10,000 ^a | Partial, 10% | 1451 ^a | Partial, 30% |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/F42H) | 190 | 3579 | Partial, 80% | 411 ^a | Full |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/F42K) | 191 | >10,000 ^a | Partial, 50% | 82 ^a | Partial, 60% |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/K43E) | 193 | 386-553 | Partial, 80-90% | 46-142 ^a | Partial, 50-0% |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/Y45A) | 195 | 62 | Partial, 90% | 300 ^a | Partial, 70% |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/Y45K) | 196 | 7951 ^a | Partial, 70% | 205 ^a | Partial, 60% |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/Y45R) | 198 | >10,000 ^a | Partial, 80% | 293 ^a | Partial, 60% |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/E61A) | 199 | 367 | Partial, 80% | 195 ^a | Partial, 60% |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/E62A) | 200 | 3265 ^a | Partial, 70% | 230 ^a | Partial, 50% |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/E62R) | 201 | >10,000 ^a | Inactive, 5% | >10,000 on graph, NC ^a | Partial, 10% |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/E62K) | 202 | >10,000 ^a | Inactive, 10% | >10,000 on graph, NC ^a | Partial, 10% |

TABLE 12-continued

| Fold change from rhIL-2 and agonistic activity on 1H3-hIgG1-L6-hIL-2 fusion proteins from Group 5 | | | | | |
|---|-------------------------------------|---------------------------------------|----------------------------------|---|--|
| Variants | SEQ ID NO of hIL-2 variant | Fold change from rhIL-2 (NK-92) | Agonistic Activity (NK-92) | Fold change from rhIL-2 (TF1 + IL-2R β) | Agonistic Activity (TF1 + IL-2R β) |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/E62Y) | 203 | >10,000 ^a | Partial, 70% | 265 ^a | Partial, 40% |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/E68Y) | 204 | 131 | Partial, 80% | 61 ^a | Partial, 50% |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/E68A) | 205 | 45 | Partial, 60% | 620 ^a | Partial, 60% |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/E68L) | 206 | 187 | Partial, 80% | 172 ^a | Partial, 40% |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/L72R) | 208 | 1178 | Full | 499 ^a | Partial, 70% |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/L72D) | 210 | >10,000 ^a | Partial, 70% | 456-504 ^a | Partial, 60-70% |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/L72H) | 211 | 798 | Partial, 70% | 117 ^a | Partial, 70% |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/F42K/Y45R) | 214 | >10,000 ^a | Partial, 60-70% | 155 185 ^a | Partial, 70% |
| 1H3-hIgG1-L6-hIL-2 (F42K/Y45R/D20A/S87A) | 213 | 840 ^a | Partial, 70% | 155 ^a | Partial, 70% |
| 1H3-hIgG1-L6-hIL-2 (D20A/R38E/C125A) | 215 | >10,000 on graph, NC ^a | Partial, 50% | 183-584 ^a | Partial, 50-70% |
| hIgG1-L6-hIL-2(T3A/D20A/R38E) | 216 | >10,000 ^a | Partial, 60-90% | 77-484 ^a | Partial, 60% |
| 1H3-hIgG1-L6-hIL-2 (T3A/D20A/R38E/C125A) | 217 | >10,000 ^a | Partial, 90% | 218-512 ^a | Partial, 50-60% |
| 1H3-hIgG1-L6-hIL-2(A1-3APT/D20A/R38E) | 218 | 24-69 | Full | 6 | Full |
| 1H3-hIgG1-L6-hIL-2 (A1- 3APT/D20A/R38E/C125A) | 219 | 49-619 | Partial, 30-70% | 165-619 ^a | Partial, 40-50% |
| 1H3-hIgG1-L6-hIL-2 (R38E/Q126D) | 225 | >10,000 on graph, NC ^a | Partial, 60% | >10,000 on graph, NC ^a | Partial, 40% |
| 1H3-hIgG1-L6-hIL-2 (F42K/Y45R/Q126D) | 228 | >10,000 ^a | Partial, 60% | 226 ^a | Partial, 50% |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/Q126D) | 229 | >10,000 on graph, NC ^a | Inactive | >10,000 on graph, NC ^a | Inactive |

NC = Not Calculated by GraphPad Prism 7

^a = Fold change is an estimate only since a full four parameter logistic curve was not reached

TABLE 13

| Fold change from rhIL-2 and agonistic activity on 1H3-hIgG1-L6-hIL-2 fusion proteins from Group 6 | | | | | |
|---|-------------------------------------|---------------------------------------|----------------------------------|---|--|
| Variants | SEQ ID NO of hIL-2 variant | Fold change from rhIL-2 (NK-92) | Agonistic Activity (NK-92) | Fold change from rhIL-2 (TF1 + IL-2R β) | Agonistic Activity (TF1 + IL-2R β) |
| 1H3-hIgG1-L6-hIL-2 (D20A/F42N) | 247 | >10,000 ^a | Partial, 60% | >10,000 on graph, NC ^a | Partial, 80% |
| 1H3-hIgG1-L6-hIL-2 (D20A/F42Q) | 248 | >10,000 ^a | Partial, 50% | 16 ^a | Partial, 70% |
| 1H3-hIgG1-L6-hIL-2 (D20A/F42P) | 254 | >10,000 ^a | Partial, 60% | 13 ^a | Partial, 80% |
| 1H3-hIgG1-L6-hIL-2 (D20A/F42S) | 255 | >10,000 ^a | Partial, 60% | 17 ^a | Partial, 40% |
| 1H3-hIgG1-L6-hIL-2 (D20A/Y45E) | 264 | 4717 | Partial, 80% | 32 ^a | Partial, 50% |
| 1H3-hIgG1-L6-hIL-2 (I92D/F42Q) | 277 | >10,000 ^a | Partial, 50% | 24 ^a | Partial, 70% |
| 1H3-hIgG1-L6-hIL-2 (I92D/F42I) | 280 | >10,000 ^a | Partial, 30% | 117 ^a | Partial, 20% |
| 1H3-hIgG1-L6-hIL-2 (I92D/F42K) | 282 | >10,000 ^a | Partial, 50% | 58 ^a | Partial, 90% |
| 1H3-hIgG1-L6-hIL-2 (I92D/F42T) | 286 | >10,000 ^a | Partial, 60% | >10,000 on graph, NC ^a | Partial, 80% |
| 1H3-hIgG1-L6-hIL-2 (R38E/D20S) | 307 | >10,000 ^a | Partial, 50% | 25 ^a | Partial, 40% |
| 1H3-hIgG1-L6-hIL-2 (F42A/N88R) | 308 | >10,000 ^a | Partial, 70% | 34 ^a | Partial, 30% |

NC = Not Calculated by GraphPad Prism

^a = Fold change is an estimate only since a full four parameter logistic curve was not reached

Example 5: Testing for Attenuation for the High-Affinity and Intermediate-Affinity hIL-2 Receptor with Cell-Based Proliferation Assays

The attenuation of IL-2 activity of antibody-attenuated hIL-2 fusion proteins from Groups 1-6 in Example 2 (2D12-mlgG1-D265A-L6-hIL-2, 2D12-hIgG1-L6-hIL-2, and 1H3-

⁶⁰ hIgG1-L6-hIL-2 fusion proteins) were tested in proliferation assays in both the NK-92 and TF1+IL-2R β cell lines as described in Protocol E. The results of the assays are provided in Tables 14-19.

⁶⁵ Selected 1H3-hIgG1-L6-hIL-2 fusion proteins with substantial attenuation in the pSTAT5 titration curves from Example 4 were tested in this cell-based proliferation assay.

pSTAT5 is a downstream read-out of IL-2 activity and assays require only 10 minutes of stimulation which may be a small snapshot of IL-2 dependent activity. For proliferation assays, cells were incubated with 2D12-mIgG1-D265A-L6-hIL-2, 2D12-hIgG1-L6-hIL-2, 1H3-hIgG1-L6-hIL-2 fusion proteins, or recombinant hIL-2 control for 3-4 days, providing a more physiological relevant read-out of IL-2 dependent activity in vivo. Other 2D12-mIgG1-D265A-L6-hIL-2 and 2D12-hIgG1-L6-hIL-2 fusion proteins that were generated but not tested in a pSTAT5 assay were assayed for IL-2 dependent activity using this proliferation assay.

Similar to cell-based pSTAT5 dose-titration experiments, the calculated EC₅₀ as determined from relative lumines-

cence units (RLU) instead of gMFI and analysis of the results were performed identically to Example 4 once EC₅₀ was calculated. Similar to results identified in Example 4, proliferation curves demonstrated that some substitutions that modulated binding to both the alpha chain and beta chain substantially attenuated IL-2 activity on the high affinity receptor in comparison to single substitutions for binding to the alpha or beta chain only. These selected 1H3-hIgG1-L6-hIL-2 fusion proteins were also tested for proliferation on the TF1+IL-2R β cell line and demonstrated that some of these same substitutions substantially attenuated IL-2 activity on the intermediate affinity receptor.

TABLE 14

Fold change from rhIL-2 and agonistic activity on 2D12-mIgG1-D265A-L6-hIL-2 or 2D12-hIgG1-L6-hIL-2 fusion proteins from Group 1 in a cell-based proliferation assay

| Variants | SEQ ID NO of hIL-2 variant | Fold change from rhIL-2 (NK-92) | Agonistic Activity (NK-92) | Fold change from rhIL-2 (TF1 + IL-2R β) | Agonistic Activity (TF1 + IL-2R β) |
|---------------------------------------|----------------------------|-----------------------------------|----------------------------|--|---|
| 2D12-mIgG1-D265A-L6-hIL-2 (F42K) | 1 | 2 | Full | 0 | Full |
| 2D12-mIgG1-D265A-L6-hIL-2 (Y45R) | 60 | 3 | Full | 2 | Full |
| 2D12-hIgG1-L6-hIL-2 (V69A) | 2 | 0 | Full | 0 | Full |
| 2D12-hIgG1-L6-hIL-2 (V69E) | 3 | 13 | Partial, 60% | 83 | Full |
| 2D12-hIgG1-L6-hIL-2 (V69H) | 6 | 41 | Partial, 60% | 544 | Full |
| 2D12-hIgG1-L6-hIL-2 (V69K) | 8 | >10,000 on graph, NC ^a | Inactive | 3033 | Partial, 40% |
| 2D12-hIgG1-L6-hIL-2 (V69L) | 9 | 1 | Full | 1 | Full |
| 2D12-hIgG1-L6-hIL-2 (V69F) | 4 | 0 | Full | 1 | Full |
| 2D12-hIgG1-L6-hIL-2 (V69G) | 5 | 108 | Full | 396 | Full |
| 2D12-hIgG1-L6-hIL-2 (V69I) | 7 | 1 | Full | 1 | Full |
| 2D12-hIgG1-L6-hIL-2 (V69M) | 10 | 2 | Full | 3 | Full |
| 2D12-hIgG1-L6-hIL-2 (V69Q) | 11 | 7 | Full | 16 | Full |
| 2D12-mIgG1-D265A-L6-hIL-2 (V69R) | 581 | 2392 | Partial, 70% | 2973 | Partial, 50% |
| 2D12-hIgG1-L6-hIL-2 (V69S) | 12 | 6 | Full | 13 | Full |
| 2D12-hIgG1-L6-hIL-2 (V69T) | 13 | 3 | Full | 3 | Full |
| 2D12-hIgG1-L6-hIL-2 (V69W) | 14 | 0 | Full | 1 | Full |
| 2D12-hIgG1-L6-hIL-2 (V69Y) | 15 | 1 | Full | 1 | Full |
| 2D12-mIgG1-D265A-L6-hIL-2 (D20A) | 31 | 1 | Full | >10,000 ^a | Full |
| 2D12-mIgG1-D265A-L6-hIL-2 (D20N) | 32 | 0 | Full | >10,000 ^a | Full |
| 2D12-mIgG1-D265A-L6-hIL-2 (D20K) | 33 | 4 | Full | >10,000 on graph, NC ^a | Inactive |
| 2D12-mIgG1-D265A-L6-hIL-2 (N88A) | 34 | 0 | Full | 2289 | Full |
| 2D12-mIgG1-D265A-L6-hIL-2 (N88G) | 35 | 0 | Full | 2978 | Full |
| 2D12-mIgG1-D265A-L6-hIL-2 (N88H) | 36 | 1-3 | Full | >10,000 on graph, NC ^a | Inactive |
| 2D12-mIgG1-D265A-L6-hIL-2 (N88K) | 37 | 564-9557 | Partial, 40% | >10,000 on graph, NC ^a | Inactive |
| 2D12-mIgG1-D265A-L6-hIL-2 (Q126L) | 375 | 0-12 | Full | 118 | Full |
| 2D12-mIgG1-D265A-L6-hIL-2 (Q126E) | 376 | 0-3 | Full | 40 | Full |
| 2D12-mIgG1-D265A-L6-hIL-2 (F42K/F44K) | 16 | 44 | Full | >10,000 on graph, NC ^a | Inactive |
| 2D12-mIgG1-D265A-L6-hIL-2 (F42K/Y45R) | 17 | 1-2 | Full | 0-3 | Full |
| 2D12-mIgG1-D265A-L6-hIL-2 (F42K/V69R) | 18 | 1500 | Partial, 80% | 841 | Partial, 80% |
| 2D12-mIgG1-D265A-L6-hIL-2 (Y45R/V69R) | 19 | 1 | Full | 3 | Full |
| 2D12-mIgG1-D265A-L6-hIL-2 (D20A/D84A) | 38 | 1 | Full | >10,000 on graph, NC ^a | Inactive |
| 2D12-mIgG1-D265A-L6-hIL-2 (D20A/E15A) | 39 | 0 | Full | >10,000 on graph, NC ^a | Partial, 40% |
| 2D12-mIgG1-D265A-L6-hIL-2 (D20A/E95A) | 40 | 0 | Full | >10,000 ^a | Full |
| 2D12-mIgG1-D265A-L6-hIL-2 (D20A/N88A) | 41 | 6 | Partial, 60% | >10,000 on graph, NC ^a | Inactive |
| 2D12-mIgG1-D265A-L6-hIL-2 (D20A/S87A) | 42 | 0 | Full | >10,000 ^a | Full |
| 2D12-mIgG1-D265A-L6-hIL-2 (D84A/N88A) | 43 | 0 | Full | >10,000 on graph, NC ^a | Inactive |
| 2D12-mIgG1-D265A-L6-hIL-2 (E15A/N88A) | 44 | 0 | Full | 4201 | Partial, 80% |

TABLE 14-continued

Fold change from rhIL-2 and agonistic activity on 2D12-mIgG1-D265A-L6-hIL-2 or 2D12-hIgG1-L6-hIL-2 fusion proteins from Group 1 in a cell-based proliferation assay

| Variants | SEQ ID NO of hIL-2 variant | Fold change from rhIL-2 (NK-92) | Agonistic Activity (NK-92) | Fold change from rhIL-2 (TF1 + IL-2R β) | Agonistic Activity (TF1 + IL-2R β) |
|---|-------------------------------------|---------------------------------------|----------------------------------|---|--|
| 2D12-mIgG1-D265A-L6-hIL-2 (S87A/N88A) | 45 | 0 | Full | 1521 | Full |
| 2D12-mIgG1-D265A-L6-hIL-2 (F42K/F44K/Y45R) | 20 | NT | NT | 0 | Full |
| 2D12-mIgG1-D265A-L6-hIL-2 (F42A/Y45A/L72G) | 574 | 0-1 | Full | 0-3 | Full |
| 2D12-mIgG1-D265A-L6-hIL-2 (R38A/F42K/Y45R) | 21 | 1 | Full | 0 | Full |
| 2D12-mIgG1-D265A-L6-hIL-2 (R38E/F42K/Y45R) | 22 | 1-3 | Full | 0 | Full |
| 2D12-mIgG1-D265A-L6-hIL-2 (K43E/F42K/Y45R) | 23 | 0 | Full | 3 | Full |
| 2D12-mIgG1-D265A-L6-hIL-2 (K43T/F42K/Y45R) | 24 | 0 | Full | 3 | Full |
| 2D12-mIgG1-D265A-L6-hIL-2 (F42K/Y45R/E62A) | 25 | 1 | Full | 0-3 | Full |
| 2D12-mIgG1-D265A-L6-hIL-2 (P65R/F42K/Y45R) | 26 | 1 | Full | 0-2 | Full |
| 2D12-mIgG1-D265A-L6-hIL-2 (P65S/F42K/Y45R) | 27 | 1 | Full | 0-2 | Full |
| 2D12-mIgG1-D265A-L6-hIL-2 (V69A/F42K/Y45R) | 28 | 1 | Full | 0-4 | Full |
| 2D12-mIgG1-D265A-L6-hIL-2 (V69D/F42K/Y45R) | 29 | 1 | Full | 0-5 | Full |
| 2D12-mIgG1-D265A-L6-hIL-2 (V69R/F42K/Y45R) | 30 | 1-4 | Full | 0-6 | Full |

NT = Not Tested

NC = Not Calculated by GraphPad Prism 7

^a = Fold change is an estimate only since a full four parameter logistic curve was not reached

TABLE 15

Fold change from rhIL-2 and agonistic activity on 1H3-hIgG1-L6-hIL-2 fusion proteins from Group 2 in a cell-based proliferation assay

| Variants | SEQ ID NO of hIL-2 variant | Fold change from rhIL-2 (NK-92) | Agonistic Activity (NK-92) | Fold change from rhIL-2 (TF1 + IL-2R β) | Agonistic Activity (TF1 + IL-2R β) |
|--|-------------------------------------|---------------------------------------|----------------------------------|---|--|
| 1H3-hIgG1-L6-hIL-2 (R38A) | 46 | 0 | Full | 1 | Full |
| 1H3-hIgG1-L6-hIL-2 (R38D) | 47 | 3 | Full | 0 | Full |
| 1H3-hIgG1-L6-hIL-2 (R38E) | 48 | 7 | Full | 1 ^a | Full |
| 1H3-hIgG1-L6-hIL-2 (F42R) | 50 | 6 | Full | 0 ^a | Full |
| 1H3-hIgG1-L6-hIL-2 (F42D) | 52 | 10 | Full | 2 | Full |
| 1H3-hIgG1-L6-hIL-2 (K43A) | 54 | 1 ^a | Full | 2 | Full |
| 1H3-hIgG1-L6-hIL-2 (Y45R) | 60 | 4 | Full | 0 ^a | Full |
| 1H3-hIgG1-L6-hIL-2 (E61A) | 61 | 0 ^a | Full | 1 | Full |
| 1H3-hIgG1-L6-hIL-2 (E61R) | 62 | 1 | Full | 1 | Full |
| 1H3-hIgG1-L6-hIL-2 (E61K) | 63 | 1 | Full | 1 | Full |
| 1H3-hIgG1-L6-hIL-2 (E62A) | 64 | 1 | Full | 1 | Full |
| 1H3-hIgG1-L6-hIL-2 (E62R) | 65 | >10,000 on graph, NC ^a | Inactive | 209 | Partial, 60% |
| 1H3-hIgG1-L6-hIL-2 (E62K) | 66 | >10,000 ^a | Partial, 40-70% | 67-99 | Partial, 60% |
| 1H3-hIgG1-L6-hIL-2 (E62Y) | 67 | 1 | Full | 1 | Full |
| 1H3-hIgG1-L6-hIL-2 (E68K) | 70 | 0 | Full | 1 | Full |
| 1H3-hIgG1-L6-hIL-2 (E68R) | 71 | 1 | Full | 1 | Full |
| 1H3-hIgG1-L6-hIL-2 (L72R) | 74 | 3 | Full | 3 | Full |
| 1H3-hIgG1-L6-hIL-2 (L72D) | 76 | 2 | Full | 0 | Full |
| 1H3-hIgG1-L6-hIL-2 (L72H) | 77 | 1 | Full | 1 | Full |
| 1H3-hIgG1-L6-hIL-2 (R38D/E61R) | 79 | 36 | Full | 2 | Full |
| 1H3-hIgG1-L6-hIL-2 (R38D/E61R/K43E) | 80 | 27 | Full | 1 | Full |

TABLE 15-continued

| Fold change from rhIL-2 and agonistic activity on 1H3-hIgG1-L6-hIL-2 fusion proteins from Group 2 in a cell-based proliferation assay | | | | | |
|---|---------------------|---------------------------------|----------------------------|--|--|
| Variants | SEQ ID | | Agonistic Activity (NK-92) | Fold change from rhIL-2 (TF1 + IL-2R β) | Agonistic Activity (TF1+ IL-2R β) |
| | NO of hIL-2 variant | Fold change from rhIL-2 (NK-92) | | | |
| 1H3-hIgG1-L6-hIL-2 (T3A/F42A/Y45A/L72G/C125A) | 81 | 142 | Full | 1-2 | Partial, 40%-Full |

NT = Not Tested

NC = Not Calculated by GraphPad Prism 7

^a = Fold change is an estimate only since a full four parameter logistic curve was not reached

TABLE 16

| Fold change from rhIL-2 and agonistic activity on 1H3-hIgG1-L6-hIL-2 fusion proteins from Group 3 in a cell-based proliferation assay | | | | | |
|---|---------------------|---------------------------------|----------------------------|--|--|
| Variants | SEQ ID | | Agonistic Activity (NK-92) | Fold change from rhIL-2 (TF1 + IL-2R β) | Agonistic Activity (TF1+ IL-2R β) |
| | NO of hIL-2 variant | Fold change from rhIL-2 (NK-92) | | | |
| 1H3-hIgG1-L6-hIL-2 (H16E) | 87 | 0 | Full | 34 | Full |
| 1H3-hIgG1-L6-hIL-2 (L19A) | 88 | NT | NT | 1 | Full |
| 1H3-hIgG1-L6-hIL-2 (D20I) | 89 | NT | NT | 8 ^a | Partial, 50% |
| 1H3-hIgG1-L6-hIL-2 (D20S) | 90 | 1 | Full | 201-304 | Partial, 80%-Full |
| 1H3-hIgG1-L6-hIL-2 (D20H) | 91 | 239 | Full | 986-6461 ^a | Partial, 50-70% |
| 1H3-hIgG1-L6-hIL-2 (D20W) | 93 | NT | NT | >10,000 on graph, NC ^a | Inactive |
| 1H3-hIgG1-L6-hIL-2 (D20Y) | 94 | 880-2097 ^a | Full | 383 | Full |
| 1H3-hIgG1-L6-hIL-2 (D20R) | 95 | NT | NT | 262-275 | Full |
| 1H3-hIgG1-L6-hIL-2 (D20F) | 96 | NT | NT | >10,000 on graph, NC ^a | Inactive |
| 1H3-hIgG1-L6-hIL-2 (D84A) | 98 | NT | NT | 21 | Full |
| 1H3-hIgG1-L6-hIL-2 (D84R) | 99 | 9 | Full | 269-455 | Partial, 80-90% |
| 1H3-hIgG1-L6-hIL-2 (D84K) | 100 | 4 | Full | 354-385 | Partial, 70%-Full |
| 1H3-hIgG1-L6-hIL-2 (N88Y) | 102 | NT | NT | >10,000 on graph, NC ^a | Inactive |
| 1H3-hIgG1-L6-hIL-2 (N88D) | 103 | 0 | Full | 115-137 | Partial, 70%-Full |
| 1H3-hIgG1-L6-hIL-2 (N88R) | 104 | 1-5 | Partial, 80%-Full | 959 | Partial, 80% |
| 1H3-hIgG1-L6-hIL-2 (N88E) | 105 | NT | NT | 1162 | Partial, 50% |
| 1H3-hIgG1-L6-hIL-2 (N88F) | 106 | NT | NT | >10,000 on graph, NC ^a | Inactive |
| 1H3-hIgG1-L6-hIL-2 (N88I) | 107 | NT | NT | >10,000 on graph, NC ^a | Inactive |
| 1H3-hIgG1-L6-hIL-2 (I92Y) | 109 | NT | NT | 1 | Full |
| 1H3-hIgG1-L6-hIL-2 (I92S) | 110 | NT | NT | 10 | Full |
| 1H3-hIgG1-L6-hIL-2 (I92R) | 112 | NT | NT | 13 | Full |
| 1H3-hIgG1-L6-hIL-2 (I92D) | 113 | 15-20 | Full | 609-1006 | Partial, 90%-Full |
| 1H3-hIgG1-L6-hIL-2 (E95R) | 116 | NT | NT | 8 | Full |
| 1H3-hIgG1-L6-hIL-2 (D20T) | 92 | 2 | Full | 124-149 | Full |
| 1H3-hIgG1-L6-hIL-2 (D20Y/H16E) | 118 | 5 | Full | 8076 ^a | Partial, 80% |

NT = Not Tested

NC = Not Calculated by GraphPad Prism 7

^a = Fold change is an estimate only since a full four parameter logistic curve was not reached

TABLE 17

| Fold change from rhIL-2 and agonistic activity on 1H3-hIgG1-L6-hIL-2 fusion proteins from Group 4 in a cell-based proliferation assay | | | | | |
|---|---------------------|---------------------------------|----------------------------|--|---|
| Variants | SEQ ID | | Agonistic Activity (NK-92) | Fold change from rhIL-2 (TF1 + IL-2R β) | Agonistic Activity (TF1 + IL-2R β) |
| | NO of hIL-2 variant | Fold change from rhIL-2 (NK-92) | | | |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (E15A) | 82 | 14 | Partial, 90% | 13 | Partial, 70% |

TABLE 17-continued

| Fold change from rhIL-2 and agonistic activity on 1H3-hIgG1-L6-hIL-2 fusion proteins from Group 4 in a cell-based proliferation assay | | | | | |
|---|----------------------------|-----------------------------------|----------------------------|--|---|
| Variants | SEQ ID NO of hIL-2 variant | Fold change from rhIL-2 (NK-92) | Agonistic Activity (NK-92) | Fold change from rhIL-2 (TF1 + IL-2R β) | Agonistic Activity (TF1 + IL-2R β) |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (D20S) | 90 | 127 | Full | 8709 ^a | Partial, 50% |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (D20W) | 93 | >10,000 on graph, NC ^a | Inactive | >10,000 on graph, NC ^a | Inactive |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (D20Y) | 94 | >10,000 on graph, NC ^a | Partial, 50% | >10,000 on graph, NC ^a | Inactive |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (D84K) | 100 | 783 | Partial, 90% | 2051 ^a | Partial, 30% |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (S87A) | 101 | 19 | Partial, 90% | 20 | Partial, 90% |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (N88D) | 103 | 50 | Full | 3284 ^a | Partial, 90% |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (N88R) | 104 | 42 | Full | 6864 ^a | Partial, 50% |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (E95K) | 117 | 51 | Full | 164 | Partial, 80% |

NC = Not Calculated by GraphPad Prism 7

^a = Fold change is an estimate only since a full four parameter logistic curve was not reached

TABLE 18

| Fold change from rhIL-2 and agonistic activity on 1H3-hIgG1-L6-hIL-2 fusion proteins from Group 5 in a cell-based proliferation assay | | | | | |
|---|----------------------------|-----------------------------------|----------------------------|--|---|
| Variants | SEQ ID NO of hIL-2 variant | Fold change from rhIL-2 (NK-92) | Agonistic Activity (NK-92) | Fold change from rhIL-2 (TF1 + IL-2R β) | Agonistic Activity (TF1 + IL-2R β) |
| 1H3-hIgG1-L6-hIL-2 (F42K/D20A) | 129 | >10,000 on graph, NC ^a | Partial, 20% | 3060 ^a | Full |
| 1H3-hIgG1-L6-hIL-2 (F42A/D20A) | 130 | >10,000 on graph, NC ^a | Full | 2081 ^a | Full |
| 1H3-hIgG1-L6-hIL-2 (R38P/D20A) | 141 | 86 | Full | 761 | Full |
| 1H3-hIgG1-L6-hIL-2 (R38S/D20A) | 142 | 140 | Full | 662 | Full |
| 1H3-hIgG1-L6-hIL-2 (R38V/D20A) | 146 | 11 | Full | 843 | Full |
| 1H3-hIgG1-L6-hIL-2 (D20A/R38E) | 149 | 1183-2016 | Partial, 70%-Full | >10,000 ^a | Partial, 80%-Full |
| 1H3-hIgG1-L6-hIL-2 (R38D/D20A) | 150 | 2262 ^a | Full | 680 | Full |
| 1H3-hIgG1-L6-hIL-2 (F42R/I92D) | 159 | >10,000 on graph, NC ^a | Partial, 30% | 1210 | Full |
| 1H3-hIgG1-L6-hIL-2 (F42H/I92D) | 160 | 288 ^a | Full | 242 ^a | Full |
| 1H3-hIgG1-L6-hIL-2 (F42A/I92D) | 161 | >10,000 on graph, NC ^a | Partial, 60% | 2275 | Partial, 80% |
| 1H3-hIgG1-L6-hIL-2 (R38D/I92D) | 170 | 746 ^a | Partial, 90% | 172 | Full |
| 1H3-hIgG1-L6-hIL-2 (R38E/I92D) | 171 | 1611 ^a | Full | 116 | Full |
| 1H3-hIgG1-L6-hIL-2 (R38E/D84R) | 175 | >10,000 on graph, NC ^a | Full | 147 | Full |
| 1H3-hIgG1-L6-hIL-2 (R38E/D84K) | 176 | >10,000 on graph, NC ^a | Partial, 70% | 315 | Full |
| 1H3-hIgG1-L6-hIL-2 (R38D/E61R/D20A) | 179 | >10,000 on graph, NC ^a | Partial, 50% | 984 | Full |
| 1H3-hIgG1-L6-hIL-2 (R38E/E61R/D20A) | 180 | >10,000 on graph, NC ^a | Full | 417 | Full |
| 1H3-hIgG1-L6-hIL-2 (R38Q/E61R/D20A) | 181 | >10,000 on graph, NC ^a | Partial, 80% | 803 | Full |
| 1H3-hIgG1-L6-hIL-2 (R38A/E61R/D20A) | 182 | >10,000 on graph, NC ^a | Partial, 60% | 1031 | Full |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/R38A) | 183 | 42 | Partial, 70% | 537 | Partial, 80% |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/R38D) | 184 | 5315 ^a | Partial, 50% | 492 | Partial, 80% |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/R38E) | 185 | >10,000 on graph, NC ^a | Full | 439 | Partial, 90% |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/R38Q) | 186 | 572 | Full | 859 | Partial, 80% |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/F42R) | 187 | 2096 | Partial, 70% | 356 | Partial, 70% |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/F42A) | 188 | 369 | Partial, 70% | 73 | Partial, 90% |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/F42D) | 189 | >10,000 on graph, NC ^a | Inactive | >10,000 on graph, NC ^a | Inactive |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/F42H) | 190 | 641 | Partial, 90% | 320 | Full |
| 1H3-hIgG1-L6-hIL-2 (D20A/E95A/F42K) | 191 | >10,000 on graph, NC ^a | Inactive | 272 | Partial, 80% |

TABLE 18-continued

| Fold change from rhIL-2 and agonistic activity on 1H3-hlgG1-L6-hIL-2 fusion proteins from Group 5 in a cell-based proliferation assay | | | | | |
|---|----------------------------|-----------------------------------|----------------------------|--|-----------------------------------|
| Variants | SEQ ID NO of hIL-2 variant | Fold change from rhIL-2 (NK-92) | Agonistic Activity (NK-92) | Fold change from rhIL-2 (TF1 + IL-2Rβ) | Agonistic Activity (TF1 + IL-2Rβ) |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/K43E) | 193 | 80 | Partial, 90% | 1876 ^a | Partial, 70% |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/Y45A) | 195 | 25 | Full | 82 | Partial, 90% |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/Y45K) | 196 | >10,000 on graph, NC ^a | Partial, 20% | 383 | Partial, 60% |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/Y45R) | 198 | >10,000 on graph, NC ^a | Inactive | 57 | Partial, 50% |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/E61A) | 199 | 306 ^a | Partial, 80% | 702 | Partial, 80% |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/E62A) | 200 | >10,000 on graph, NC ^a | Partial, 20% | 661 | Partial, 60% |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/E62R) | 201 | >10,000 on graph, NC ^a | Inactive | >10,000 on graph, NC ^a | Inactive |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/E62K) | 202 | >10,000 on graph, NC ^a | Inactive | >10,000 on graph, NC ^a | Inactive |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/E62Y) | 203 | 721 | Partial, 40% | 982 ^a | Partial, 30% |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/E68Y) | 204 | 11 | Full | 469 | Full |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/E68A) | 205 | 6 | Partial, 50% | 535 | Partial, 80% |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/E68L) | 206 | 15 | Full | 972 | Partial, 60% |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/L72R) | 208 | 655 ^a | Partial, 50% | 316 | Partial, 40% |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/L72D) | 210 | 5415 | Inactive | 125 | Partial, 90% |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/L72H) | 211 | 583 ^a | Partial, 60% | 135 | Partial, 80% |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/F42K/Y45R) | 214 | >10,000 on graph, NC ^a | Inactive | 58-209 | Partial, 40-80% |
| 1H3-hlgG1-L6-hIL-2 (F42K/Y45R/D20A/S87A) | 213 | 123 | Full | 0 | Full |
| 1H3-hlgG1-L6-hIL-2 (D20A/R38E/C125A) | 215 | >10,000 ^a | Partial, 30-90% | 2102 ^a | Partial, 80% |
| 1H3-hlgG1-L6-hIL-2 (T3A/D20A/R38E) | 216 | 2338-5870 | Partial, 80%-Full | 353-571 | Full |
| 1H3-hlgG1-L6-hIL-2 (T3A/D20A/R38E/C125A) | 217 | >10,000 ^a | Full | 1086 ^a | Partial, 80%-Full |
| 1H3-hlgG1-L6-hIL-2 (Δ1-3APT/D20A/R38E) | 218 | 4-16 | Full | 32 | Partial, 90% |
| 1H3-hlgG1-L6-hIL-2 (Δ1-3APT/D20A/R38E/C125A) | 219 | >10,000 ^a | Inactive-Partial, 50% | 993 ^a | Partial, 60% |
| 1H3-hlgG1-L6-hIL-2 (F42K/Y45R/Q126D) | 228 | >10,000 ^a | Partial, 50% | 597 | Partial, 80% |
| 1H3-hlgG1-L6-hIL-2 (D20A/E95A/Q126D) | 229 | 106 ^a | Inactive | >10,000 on graph, NC ^a | Inactive |

NC = Not Calculated by GraphPad Prism 7

^a = Fold change is an estimate only since a full four parameter logistic curve was not reached

TABLE 19

| Fold change from rhIL-2 and agonistic activity on 1H3-hlgG1-L6-hIL-2 fusion proteins from Group 6 in a cell-based proliferation assay | | | | | |
|---|----------------------------|-----------------------------------|----------------------------|--|-----------------------------------|
| Variants | SEQ ID NO of hIL-2 variant | Fold change from rhIL-2 (NK-92) | Agonistic Activity (NK-92) | Fold change from rhIL-2 (TF1 + IL-2Rβ) | Agonistic Activity (TF1 + IL-2Rβ) |
| 1H3-hlgG1-L6-hIL-2 (D20A/E61R) | 230 | 3950 ^a | Partial, 10% | 278 | Partial, 50% |
| 1H3-hlgG1-L6-hIL-2 (D20A/F42L) | 247 | >10,000 ^a | Partial, 50% | 662 | Partial, 80% |
| 1H3-hlgG1-L6-hIL-2 (D20A/F42Q) | 248 | >10,000 on graph, NC ^a | Partial, 30% | 630 | Partial, 80% |
| 1H3-hlgG1-L6-hIL-2 (D20A/F42I) | 251 | 1307 ^a | Partial, 20% | 494 | Partial, 60% |
| 1H3-hlgG1-L6-hIL-2 (D20A/F42L) | 252 | 68 | Full | 533 | Partial, 60% |
| 1H3-hlgG1-L6-hIL-2 (D20A/F42M) | 253 | 53 | Full | 370 | Partial, 50% |
| 1H3-hlgG1-L6-hIL-2 (D20A/F42P) | 254 | 9374 ^a | Partial, 80% | 702 | Partial, 80% |
| 1H3-hlgG1-L6-hIL-2 (D20A/F42S) | 255 | 1286 | Partial, 70% | 687 | Partial, 70% |
| 1H3-hlgG1-L6-hIL-2 (D20A/F42T) | 256 | 1474 ^a | Partial, 10% | 622 | Partial, 80% |
| 1H3-hlgG1-L6-hIL-2 (D20A/F42W) | 257 | 414 ^a | Partial, 70% | 400 | Partial, 70% |
| 1H3-hlgG1-L6-hIL-2 (D20A/F42S) | 258 | 322 | Partial, 70% | 545 | Partial, 70% |
| 1H3-hlgG1-L6-hIL-2 (D20A/F42V) | 259 | 5796 ^a | Partial, 30% | 579 | Partial, 80% |
| 1H3-hlgG1-L6-hIL-2 (D20A/Y45A) | 260 | 61 | Partial, 80% | 554 | Partial, 80% |
| 1H3-hlgG1-L6-hIL-2 (D20A/Y45N) | 261 | 31 | Full | 390 | Partial, 70% |
| 1H3-hlgG1-L6-hIL-2 (D20A/Y45D) | 262 | 363 | Partial, 60% | 729 | Partial, 70% |
| 1H3-hlgG1-L6-hIL-2 (D20A/Y45Q) | 263 | 730 ^a | Partial, 70% | 348 | Partial, 70% |
| 1H3-hlgG1-L6-hIL-2 (D20A/Y45E) | 264 | 1414 ^a | Partial, 60% | 486 | Partial, 70% |
| 1H3-hlgG1-L6-hIL-2 (D20A/Y45G) | 265 | 613 ^a | Partial, 80% | 392 | Partial, 60% |
| 1H3-hlgG1-L6-hIL-2 (D20A/Y45H) | 266 | 420 ^a | Partial, 70% | 427 | Partial, 60% |
| 1H3-hlgG1-L6-hIL-2 (D20A/Y45I) | 267 | 39 | Partial, 70% | 137 | Partial, 30% |
| 1H3-hlgG1-L6-hIL-2 (D20A/Y45L) | 268 | 11 | Full | 426 | Partial, 70% |

TABLE 19-continued

| Fold change from rhIL-2 and agonistic activity on 1H3-hlgG1-L6-hIL-2 fusion proteins from Group 6 in a cell-based proliferation assay | | | | | |
|---|----------------------------|-----------------------------------|----------------------------|--|---|
| Variants | SEQ ID NO of hIL-2 variant | Fold change from rhIL-2 (NK-92) | Agonistic Activity (NK-92) | Fold change from rhIL-2 (TF1 + IL-2R β) | Agonistic Activity (TF1 + IL-2R β) |
| 1H3-hlgG1-L6-hIL-2 (D20A/Y45M) | 269 | 107 | Full | 449 | Partial, 60% |
| 1H3-hlgG1-L6-hIL-2 (D20A/Y45F) | 270 | 25 | Partial, 90% | 272 | Partial, 50% |
| 1H3-hlgG1-L6-hIL-2 (D20A/Y45P) | 271 | 577 ^a | Full | 710 | Full |
| 1H3-hlgG1-L6-hIL-2 (I92D/F42Q) | 277 | 7227 ^a | Partial, 30% | 872 | Full |
| 1H3-hlgG1-L6-hIL-2 (I92D/F42I) | 280 | 4587 ^a | Partial, 10% | 3644 ^a | Full |
| 1H3-hlgG1-L6-hIL-2 (I92D/F42K) | 282 | >10,000 ^a | Partial, 20% | 848 ^a | Full |
| 1H3-hlgG1-L6-hIL-2 (I92D/F42T) | 286 | >10,000 ^a | Partial, 40% | 1068 ^a | Full |
| 1H3-hlgG1-L6-hIL-2 (I92D/F42W) | 287 | 405 ^a | Full | 3954 ^a | Full |
| 1H3-hlgG1-L6-hIL-2 (I92D/F42Y) | 288 | 58 | Full | 106 | Full |
| 1H3-hlgG1-L6-hIL-2 (I92D/F42V) | 289 | 1075 ^a | Partial, 60% | 343 | Full |
| 1H3-hlgG1-L6-hIL-2 (I92D/Y45A) | 290 | 15 | Full | 285 | Full |
| 1H3-hlgG1-L6-hIL-2 (I92D/Y45Q) | 293 | 53 | Full | 80 | Full |
| 1H3-hlgG1-L6-hIL-2 (I92D/Y45G) | 295 | 41 | Full | 91 | Full |
| 1H3-hlgG1-L6-hIL-2 (I92D/Y45M) | 299 | 7 | Full | 146 | Full |
| 1H3-hlgG1-L6-hIL-2 (I92D/Y45F) | 300 | 33 | Full | 1650 ^a | Full |
| 1H3-hlgG1-L6-hIL-2 (I92D/Y45S) | 302 | 20 | Full | 306 | Full |
| 1H3-hlgG1-L6-hIL-2 (R38E/D20H) | 306 | 13 | Inactive | 2945 | Partial, 40% |
| 1H3-hlgG1-L6-hIL-2 (R38E/D20S) | 307 | >10,000 on graph, NC ^a | Partial, 50% | 626 | Full |
| 1H3-hlgG1-L6-hIL-2 (F42A/N88R) | 308 | 8351 ^a | Partial, 70% | 1456 | Full |
| 1H3-hlgG1-L6-hIL-2 (F42A/N88D) | 309 | 1966 ^a | Full | 86 | Full |
| 1H3-hlgG1-L6-hIL-2 (R38E/I92K) | 334 | >10,000 ^a | Partial, 70% | 239 | Full |
| 1H3-hlgG1-L6-hIL-2 (R38E/I92P) | 337 | >10,000 on graph, NC ^a | Inactive | >10,000 on graph, NC ^a | Inactive |
| 1H3-hlgG1-L6-hIL-2 (R38E/H16E) | 343 | 658 ^a | Full | 58 | Full |
| 1H3-hlgG1-L6-hIL-2 (R38K/D20A) | 344 | 66 | Full | 369 | Partial, 70% |

NC = Not Calculated by GraphPad Prism 7

^a = Fold change is an estimate only since a full four parameter logistic curve was not reached

Example 6: Generation of Anti-hPD-1 Antibodies

Several approaches were used to generate a variety of different anti-hPD-1 antibodies with desired properties.

In one approach, anti-hPD-1 human monoclonal antibodies were generated using transgenic chickens (OmniChicken™) that express human antibody genes (human light chain (VLCL or VKCK) and human VH) and the chicken constant regions of the heavy chain (Ching et al., mAbs 2018). Transgenic chickens were immunized with 100 μ g of Fc-tagged human PD-1 protein (huPD-1-Fc) (SEQ ID NO: 380) every 14 days for 14 weeks. In another approach, transgenic chickens were genetically immunized six times with DNA encoding human PD-1 (SEQ ID NO: 347) followed by a final boost with 100 μ g huPD-1-Fc (SEQ ID NO: 380). The serum immune response of each animal was monitored by ELISA against biotinylated human PD-1 on streptavidin coated plates.

Splenocytes were isolated from each immunized animal, tested for positive antibody clones using the Gel Encapsulated Microenvironment (GEM) assay (as described in Mettler Izquierdo, S., Varela, S., Park, M., Collarini, E. J., Lu, D., Pramanick, S., Rucker, J., Lopalco, L., Etches, R., & Harriman, W. (2016). High-efficiency antibody discovery achieved with multiplexed microscopy. *Microscopy (Oxford, England)*, 65 (4), 341-352) and screened against human PD-1 labelled beads. Positive clones were sequenced and variable regions of the heavy and light chains were cloned, assembled into a single chain variable fragment, and fused to the hinge and Fc regions of immunoglobulins (ScFv-Fc). These unique scFv-Fc fusion proteins were transiently expressed in Expi293 cells and supernatants were tested for binding activity by ELISA on plates coated with huPD-1-Fc (SEQ ID NO: 380) or cynomolgous-PD-1-Fc

(SEQ ID NO: 381). In total, 102 unique anti-human PD-1 variable heavy and variable light pairings were identified using this method. 2H7-hIgG4 (SEQ ID NOs: 382-391, 424, and 425) and A2-hIgG4 (SEQ ID NOs: 402-411, 428, and 429) were among the antibodies identified in this approach.

Other approaches led to the identification of an anti-hPD-1 antibody denoted as C51E6-hIgG4, which was germ-line optimized to become the antibody designated C51E6-5-hIgG4 (SEQ ID NOs: 392-401, 426, 427), and humanized and further sequence optimized to become the antibody designated AbzImod-hIgG4 (SEQ ID NOs: 449, 450).

The anti-PD-1 variable region sequences were expressed as human IgG4 kappa antibodies and were evaluated for the ability to bind to PD-1 expressing cells using flow cytometry as described in General Methods Protocol A. Antibodies to be tested were first screened for binding to human PD-1 using a Jurkat cell line expressing recombinant human PD-1 (Jurkat+hPD-1 cell line). Antibodies were serially diluted from a top concentration of 280 nM and Allophycocyanin-conjugated anti-human IgG secondary antibody was then added to cells for detection. Of 92 hits, 79 test anti-PD-1 antibodies had an EC₅₀ binding (by flow cytometry) of <30 nM. 2H7-hlgG4 (SEQ ID NOs: 382-391, 424, and 425), C51E6-5-hlgG4 (SEQ ID NOs: 392-401, 426, and 427), A2-hlgG4 (SEQ ID NOs: 402-411, 428, and 429), OMC.1.B6-hlgG4 (SEQ ID NOs: 438 and 439), OMC.1.D6-hlgG4 (SEQ ID NOs: 442 and 443), OMC.2.C6-hlgG4 (SEQ ID NOs: 440 and 441), 1H9-hlgG4 (SEQ ID NOs: 576 and 525), 1D5-hlgG4 (SEQ ID NOs: 577 and 527), and 2A3.H7-hlgG4 (SEQ ID NOs: 424 and 523) were among a group of antibodies identified as antibodies with medium to high affinity binding to hPD-1 using a Jurkat cell line expressing human PD-1 (SEQ ID NO: 346). The calculated EC₅₀ of binding to Jurkat cells which recombinantly

expressed hPD-1 by flow cytometry in multiple experiments was 0.1-0.3 nM for 2H7-hIgG4, 1H9-hIgG4, 1D5-hIgG4, and 2A3.H7-hIgG4. The calculated EC₅₀ of binding to Jurkat cells expressing hPD-1 by flow for C51E6-5-hIgG4 was 2-4 nM, and 3-16 nM for A2-hIgG4, OMC.1.B6-hIgG4, OMC.1.D6-hIgG4, and OMC.2.C6-hIgG4. Binding was specific to hPD-1 since 2H7-hIgG4, C51E6-5-hIgG4, A2-hIgG4, 1H9-hIgG4, 1D5-hIgG4, 2A3.H7-hIgG4, OMC.1.B6-hIgG4, OMC.1.D6-hIgG4, and OMC.2.C6-hIgG4 antibody titrations did not bind the parental Jurkat cell line which did not express hPD-1 (data not shown).

Example 7: Characterization of Anti-hPD-1 Antibody Binding in the Presence of Anti-hPD-1 #1-mIgG2b-N297A and Anti-hPD-1 #2-mIgG2b-N297A Antibodies

2H7-hIgG4, C51E6-5-hIgG4, and A2-hIgG4 were assessed for binding competition to hPD-1 in the presence of anti-hPD-1 #1-mIgG2b-N297A and anti-hPD-1 #2-mIgG2b-N297A as described in General Methods Protocol B.

As a control, OPDIVO® (nivolumab) was titrated in the presence of saturating concentrations of 10 μ M anti-hPD-1 #1-mIgG2b-N297A (FIG. 4A). The dose-titration curve in the presence of anti-hPD-1 #1-mIgG2b-N297A competitor was greatly reduced (100 to 1000-fold shift of the dose-titration curve to the right of the graph) when compared to the dose-titration curve of OPDIVO® without anti-hPD-1 #1-mIgG2b-N297A competitor. The addition of anti-hPD-1 #1-mIgG2b-N297A or anti-hPD-1 #2-mIgG2b-N297A at saturating concentrations (10 μ M) prior to exposure with 2H7-hIgG4, C51E6-5-hIgG4, or A2-hIgG4 did not abrogate binding of 2H7-hIgG4, C51E6-5-hIgG4, or A2-hIgG4 to hPD-1 as illustrated by less than 10-fold shift in FIG. 4B-4D, suggesting that 2H7-hIgG4, C51E6-5-hIgG4 and A2-hIgG4 did not compete for binding to PD-1 in the presence of anti-hPD-1 #1-mIgG2b-N297A or anti-hPD-1 #2-mIgG2b-N297A.

Example 8: Characterization of Non-Antagonist hPD-1 Antibodies

Anti-hPD-1 antibodies 2H7-hIgG4, C51E6-5-hIgG4 and A2-hIgG4 were tested for PD-1 antagonist activity using an in vitro cell-based human PD-1/PD-L1 blockade bioassay as described in General Methods Protocol C. All antibodies except A2-hIgG4 were tested at 200 nM final concentration. A2-hIgG4 was tested at 500 nM final concentration.

None of the anti-hPD-1 antibodies 2H7-hIgG4, C51E6-5-hIgG4, A2-hIgG4, OMC.1.B6-hIgG4, OMC.1.D6-hIgG4, OMC.2.C6-hIgG4, 1H9-hIgG4, 1D5-hIgG4, and 2A3.H7-hIgG4 demonstrated hPD-1 antagonist activity, as all displayed luminescence levels of an average of 3000 relative luminescence units (RLU) and exhibited an RLU similar to

the negative control KLH-C3-hIgG4 (data not shown). In contrast, the anti-hPD-1 #1, which is a known hPD-1 antagonist that blocks hPD-L1 (SEQ ID NO: 584) engagement with hPD-1, exhibited luminescence of above 14,000 RLU (data not shown).

Example 9: Anti-hPD-1-Attenuated hIL-2 Fusion Proteins Bind Jurkat Cells Expressing Human PD-1

In order to construct various antibody and antibody-attenuated hIL-2 fusion protein expression vectors, the corresponding polynucleotide encoding sequences of antibody, cytokines, cytokine receptors and linkers were generated and cloned into expression vectors. The antibodies or antibody fusion proteins were transiently expressed in Human Embryonic Kidney (HEK) 293 cells, then purified by affinity chromatography using Protein A- or Protein G-Sepharose. The purified proteins were concentrated and buffer-exchanged to phosphate buffered saline or phosphate buffered saline containing 100 mM L-arginine and 10 mM L-histidine using ultracentrifugal filtration, after which protein concentration was determined.

In some approaches, 2H7-hIgG4, C51E6-5-hIgG4, and A2-hIgG4 carrying an S228P hinge stabilization mutation were directly fused (df) to hIL-2 or fused to hIL-2 at the C-terminus of the immunoglobulin heavy chain using the L6 linker. An illustration of these anti-PD-1-attenuated hIL-2 fusion proteins is summarized in FIG. 5. Various constructs were generated with the substitutions in hIL-2 that attenuated hIL-2 activity as described in Example 2. Anti-hPD-1-attenuated hIL-2 fusion proteins listed in Table 20 were tested for binding to hPD-1 using the Jurkat cell line expressing hPD-1 as described in General Methods Protocol A. The variable region of 2H7-hIgG4 (SEQ ID NOs: 384 and 385) was further optimized, and the isotype was switched to a human IgG1 with the effector function null substitutions L235A/G237A (LAGA, as described in WO1998/006248) to become H7-632-hIgG1-LAGA (SEQ ID NOs: 414 and 415). The optimized H7-632-hIgG1-LAGA was also directly fused (df) to a variant of hIL-2 with attenuated hIL-2 activity (hIL-2 T3A/D20A/R38E/C125A; SEQ ID NO: 217) to become H7-767 (SEQ ID NOs: 412-413, 415-423, 532) and both H7-632-hIgG1-LAGA and H7-767 were tested for binding to hPD-1 (Table 20). EC₅₀ values were calculated from the geometric mean fluorescent intensity (gMFI) across the titrated concentrations using GraphPad Prism 7 software.

The generation of anti-hPD-1-attenuated hIL-2 fusion proteins did not reduce binding to hPD-1, and the anti-hPD-1-attenuated hIL-2 fusion proteins were still able to bind to Jurkat cells expressing human PD-1. The calculated EC₅₀ of tested anti-hPD-1-attenuated hIL-2 fusion proteins in comparison to respective anti-hPD-1 antibody without the attenuated hIL-2 moiety is summarized in Table 20.

TABLE 20

| Anti-hPD-1-attenuated hIL-2 fusion protein binding (EC ₅₀) to hPD-1 expressing Jurkat cell line by flow cytometry | | | |
|---|-----------------------|---|-----------------------|
| Anti-hPD-1 Antibody | EC ₅₀ (nM) | Corresponding Anti-hPD-1-hIL-2 Fusion Protein | EC ₅₀ (nM) |
| Anti-hPD-1 #1 | 0.3586 | Anti-hPD-1 #1-hIgG4-L6-hIL-2 (D20A/R38E) | 0.5318 |
| C51E6-5-hIgG4 | 2.048 | C51E6-5-hIgG4-L6-hIL-2 (D20A/R38E) | 1.587 |
| OMC.1.B6-hIgG4 | 7.422 | OMC.1.B6-hIgG4-L6-hIL-2 (D20A/R38E) | 5.635 |
| OMC.2.C6-hIgG4 | 11.52 | OMC.2.C6-hIgG4-L6-hIL-2 (D20A/R38E) | 16.32 |
| OMC.1.D6-hIgG4 | 15.96 | OMC.1.D6-hIgG4-L6-hIL-2 (D20A/R38E) | 8.87 |

TABLE 20-continued

| Anti-hPD-1-attenuated hIL-2 fusion protein binding (EC ₅₀) to hPD-1 expressing Jurkat cell line by flow cytometry | | | |
|---|-----------------------|---|-----------------------|
| Anti-hPD-1 Antibody | EC ₅₀ (nM) | Corresponding Anti-hPD-1-hIL-2 Fusion Protein | EC ₅₀ (nM) |
| A2-hIgG4 | 5.968 | A2-hIgG4-df-hIL-2 (D20A/R38E) | 10.67 |
| D12-hIgG4 | 9.674 | D12-hIgG4-df-hIL-2 (D20A/R38E) | 17.09 |
| G12-hIgG4 | 5.36 | G12-hIgG4-df-hIL-2 (D20A/R38E) | 7.578 |
| 2H7-hIgG4 | 0.2769 | 2H7-hIgG4-df-hIL-2 (D20A/R38E) | 0.1946 |
| H7-632-hIgG1-LAGA | 0.115 | H7-767 | 0.218 |

The addition of the attenuated hIL-2 moiety on anti-hPD-1 antibodies did not abrogate binding to human PD-1 as demonstrated by a less than 2-fold increase in EC₅₀ binding of anti-hPD-1-hIL-2 fusion proteins to Jurkat+hPD-1 cells in comparison to the anti-hPD-1 antibody without the attenuated hIL-2 moiety.

Example 10: Anti-hPD-1-Attenuated hIL-2 Fusion Proteins Bind hPD-1 in the Presence of Anti-hPD-1 #1 and Anti-hPD-1 #2 Antibodies

Anti-hPD-1-attenuated hIL-2 fusion proteins were tested for binding to the hPD-1 receptor in the presence of anti-hPD-1 #1 and anti-hPD-1 #2 as described in General Methods Protocol B and Example 7. The converse experiment was also performed in which anti-hPD-1 #1-mIgG2b-N297A or anti-hPD-1 #2-mIgG2b-N297A was examined for binding to hPD-1 in the presence of saturating concentrations of test antibody-attenuated hIL-2 fusion proteins. In this format, Jurkat cells expressing hPD-1 were plated at 100,000 cells per well in FACS buffer, blocked with anti-human FcγR Blocking Reagent (Miltenyi) for 10 minutes at 4° C. and washed. Test antibody-attenuated hIL-2 fusion proteins 2H7-hIgG4-df-hIL-2 (D20A/R38E), C51E6-5-hIgG4-L6-hIL-2 (D20A/R38E), A2-hIgG4-df-hIL-2 (D20A/R38E), H7-767, and isotype control anti-DNase 1H3-hIgG4-df-hIL-2 (D20A/R38E) were diluted to 280 nM final concentration in 100 μL FACS buffer and incubated with Jurkat cells expressing hPD-1 cells for 1 hour on ice. Cells were washed and re-suspended in FACS buffer containing six-fold serial titrations of anti-hPD-1 #1-mIgG2b-N297A or anti-hPD-1 #2-mIgG2b-N297A starting at a maximum concentration of 50 nM for 1 hour on ice. Cells were washed and re-suspended in 1:100 dilution of Phycoerythrin-conjugated anti-mouse IgG light chain kappa monoclonal antibody for 45 minutes on ice. Cells were again washed and re-suspended in FACS buffer with 1:1000 dilution of Sytox Green (Thermo Fisher). Flow cytometry analysis was performed using the BD FACS Canto II (BD Biosciences) and gMFI calculated using FlowJo software version 10. EC₅₀ values were calculated from the gMFI of the Phycoerythrin signal across the titrated concentrations using GraphPad Prism 7 software.

The addition of the attenuated hIL-2 to anti-hPD-1 antibodies 2H7-hIgG4, C51E6-5-hIgG4, and A2-hIgG4 did not diminish the ability of the anti-hPD-1 proteins to bind to human PD-1 in the presence of anti-hPD-1 #1-mIgG2b-N297A or anti-hPD-1 #2-mIgG2b-N297A, similar to the results described in Example 7 (FIG. 16B-16D). H7-767 was also tested in this competition assay and FIG. 13B illustrates that H7-767 continues to bind to the hPD-1 receptor in the presence of anti-hPD-1-#1-mIgG2b-N297A or anti-hPD-1 #2-mIgG2b-N297A. In contrast, the binding of the positive control anti-hPD-1 #1 was substantially decreased in the

presence of anti-hPD-1 #1-mIgG2b-N297A or anti-hPD-1 #2-mIgG2b-N297A (FIG. 16A, 13A).

FIG. 6A and FIG. 6B show that for the converse competition assay, anti-hPD-1 #1-mIgG2b-N297A (FIG. 6A) and anti-hPD-1 #2-mIgG2b-N297A (FIG. 6B) were still able to bind to hPD-1 on Jurkat cells in the presence of saturating (280 nM) anti-hPD-1-attenuated hIL-2 fusion proteins 2H7-hIgG4-df-hIL-2 (D20A/R38E), C51E6-5-hIgG4-df-hIL-2 (D20A/R38E) or A2-hIgG4-df-hIL-2 (D20A/R38E). These binding curves with saturating anti-hPD-1-attenuated hIL-2 fusion proteins prior to exposure with anti-hPD-1 fusion proteins overlapped with binding curves of anti-hPD-1 #1-mIgG2b-N297A (no competition) or anti-hPD-1 #2-mIgG2b-N297A (no competition). The binding curves also overlapped with a saturating negative control fusion protein, 1H3-hIgG4-df-hIL-2 (D20A/R38E) that did not bind to hPD-1.

Example 11: Anti-hPD-1-Attenuated hIL-2 Fusion Proteins Bind Recombinantly-Expressed Cynomolgus PD-1

Anti-hPD-1-attenuated hIL-2 fusion proteins were tested in flow cytometry for binding to cynomolgus PD-1 using a human Embryonic Kidney 293 cell line expressing the SV40 large T cell antigen (HEK-293T) that was transiently transfected to recombinantly express cynomolgus PD-1. For each transfection reaction, 2 million HEK-293T cells were transfected with 2 μg of pCMV6-hygro-HA-cyno-PD-1 (1-185) (SEQ ID NO: 448), a mammalian vector comprising the cynomolgus PD-1 extracellular domain tagged with a human influenza hemagglutinin and the sequence encoding for hygromycin resistance. Transfection was performed by electroporation. Transfected cells were blocked with human FcγR blocking reagent and stained with titrating amounts of anti-hPD-1-attenuated hIL-2 fusion proteins. Additionally, Phycoerythrin conjugated anti-hemagglutinin clone 15B12 was added to cells to stain for transfected cells and Allophycocyanin-conjugated anti-human IgG Fc secondary clone HP6017 (BioLegend Cat #409306) was added to cells to stain bound antibody. The cells were analyzed on the BD Canto II and FlowJo software version 10 was used to gate on live, transfected (hemagglutinin-positive) cells and to calculate gMFI of the Allophycocyanin signal. EC₅₀ values were calculated from the gMFI across the titrated concentrations using GraphPad Prism 7 software.

Anti-hPD-1-attenuated hIL-2 fusion proteins bound to cynomolgus PD-1-expressing HEK-293T cells in a similar fashion to the binding profile seen on Jurkat T cells expressing human PD-1 (FIG. 17). The EC₅₀ for binding to cynomolgus PD-1 expressing HEK-293T cells was 5 nM for 2H7-hIgG4-df-hIL-2 (D20A/R38E), 6 nM for C51E6-5-hIgG4-df-hIL-2 (D20A/R38E), and 11 nM for A2-hIgG4-df-hIL-2 (D20A/R38E). Anti-hPD-1 #1 and anti-hPD-1 #2

which were formatted as comparator anti-hPD-1-attenuated hIL-2 fusion proteins also bound to cynomolgus PD-1 with EC_{50} values of 9 nM and 2 nM, respectively, suggesting that the addition of the attenuated hIL-2 moiety on the anti-hPD-1 antibodies did not abrogate binding to cynomolgus PD-1.

Example 12: Anti-hPD-1-Attenuated hIL-2 Fusion Proteins Bind Activated Primary Human and Cynomolgus PD-1

The binding of anti-hPD-1 antibodies and anti-hPD-1-attenuated hIL-2 fusion proteins on activated primary T cells expressing hPD-1 was examined by flow cytometry. To test if 2H7-hIgG4, C51E6-5-hIgG4, or A2-hIgG4 bound to native hPD-1, cryopreserved human peripheral blood mononuclear cells (PBMCs) were thawed and activated with 50 ng/ml phorbol 12-myristate 13-acetate (PMA) and 1 μ g/mL ionomycin to up-regulate the hPD-1 receptor. Activated PBMCs were collected, blocked with 1:50 dilution of Human Fc γ R Blocking Reagent (Miltenyi) for 10 minutes at 4° C., and stained with titrated concentrations of anti-hPD-1 antibodies 2H7-hIgG4, C51E6-5-hIgG4, A2-hIgG4, anti-hPD-1 #1, and isotype control. Cells were then stained with 1:20 dilution of Allophycocyanin-conjugated anti-human IgG Fc to detect bound antibody. To delineate immune subsets, a cocktail of surface markers included anti-human CD3, anti-CD4, and anti-CD8 antibodies was used. In addition, a sample fraction was examined for cellular expression of hPD-1, hCD25, hCD122, and hCD132. Cells were analyzed on the BD Fortessa (BD Biosciences), FlowJo software version 10 was used to gate on T cell subsets then calculate gMFI of the allophycocyanin signal. EC_{50} values were calculated from the gMFI across the titrated concentrations using GraphPad Prism 7 software. To test the binding of anti-hPD-1-hIL-2 fusion proteins, cryopreserved CD3+ T cells were activated with PMA/ionomycin and flow cytometry binding was performed identically as described above.

Human PD-1 antibody-attenuated hIL-2 fusion proteins were also tested for binding to activated cynomolgus T cells using flow cytometry. Cynomolgus PBMCs were activated with a mixture of 0.081 μ M PMA and 1.34 μ M ionomycin. 24 hours later, cells were stained using the same procedure as binding to human PD-1 primary cells described above except cynomolgus cross-reactive markers were used. FlowJo software version 10 was used to gate on live, CD3+CD4+ or CD3+CD8+ T cells and then to calculate gMFI of the Allophycocyanin signal. EC_{50} values were calculated from the gMFI across the titrated concentrations of anti-hPD-1 antibodies or hPD-1 antibody-attenuated hIL-2 fusion proteins using GraphPad Prism 7 software.

In some variants tested, the attenuated hIL-2 also included the substitutions T3A and C125A, which remove a site for O-linked glycosylation and substitute away a free cysteine residue, respectively.

40-50% of CD4+ T cells were PD-1+ while 30-40% of CD8+ T cells were PD-1+ after PMA and ionomycin activation (data not shown). The calculated EC_{50} for binding to activated human CD3+CD4+ T cells by flow cytometry was 0.1-0.7 nM for 2H7-hIgG4, 12 nM for C51E6-5-hIgG4, 30 nM for A2-hIgG4, and 0.04 nM for 2H7-hIgG4-df-hIL-2 (T3A/D20A/R38E/C125A). The EC_{50} for binding to activated human CD3+CD8+ T cells was 0.1-0.8 nM for 2H7-hIgG4, 16 nM for C51E6-5-hIgG4, 22 nM for A2-hIgG4, and 0.03 nM for 2H7-hIgG4-df-hIL-2 (T3A/D20A/R38E/C125A). The EC_{50} for binding to activated human CD3+

CD4+ T cells was 0.19 nM and activated human CD3+CD8+ T cells was 0.12 nM for H7-767. The EC_{50} for binding to activated cynomolgus CD3+CD4+ T cells was 0.09 nM for 2H7-hIgG4 and 0.04 nM for 2H7-hIgG4-df-hIL-2 (T3A/D20A/R38E/C125A). EC_{50} for binding to activated cynomolgus CD3+CD8+ T cells was 0.08 nM for 2H7-hIgG4 and 0.03 nM for 2H7-hIgG4-df-hIL-2 (T3A/D20A/R38E/C125A). The EC_{50} for binding to activated cynomolgus CD3+CD4+ T cells was 0.26 nM and activated cynomolgus CD3+CD8+ T cells was 0.24 nM for H7-767. This data demonstrated that when the hPD-1 antibodies were converted to anti-hPD-1-attenuated hIL-2 fusion proteins, the calculated EC_{50} value for binding to activated hPD-1 remained similar to the calculated EC_{50} value of hPD-1 naked antibody binding to hPD-1. H7-767 and H7-632-hIgG1-LAGA anti-PD-1 naked antibody were tested for binding on primary non-activated human CD4+ and CD8+ T cells by flow cytometry. Frozen human CD3+ T were thawed and flow cytometry performed as described above. Both H7-767 and H7-632-hIgG1-LAGA anti-PD-1 naked antibody did not bind non-activated human CD4+ and CD8+ T cells (data not shown).

Example 13: Quantification of Binding of Anti-hPD-1 Antibodies and Anti-hPD-1-Attenuated hIL-2 Fusion Proteins to Recombinant Human or Cynomolgus PD-1 by Surface Plasmon Resonance (SPR)

Surface plasmon resonance binding analysis was performed using a high-throughput SPR Carterra® LSA™ to determine binding affinities of anti-hPD-1 antibodies and anti-hPD-1-attenuated hIL-2 fusion proteins. Proteins were diluted to 2 or 10 μ g/mL in 10 mM sodium acetate pH 4.5 containing 0.01% Tween-20 and coupled to a HC30M (Carterra Bio) chip using sulpho-N-hydroxysuccinimide/1-ethyl-3-(3-dimethylamino) propyl carbodiimide (sulpho-NHS/EDC) coupling chemistry and blocked with ethanolamine. A non-regenerative kinetic coupling process was used to determine binding kinetics to commercially sourced recombinant His-tagged human PD-1 and His-tagged cynomolgus PD-1 (Acro Biosystems).

Anti-hPD-1 antibodies and anti-hPD-1-attenuated hIL-2 fusion proteins were expressed with either a modified human IgG1 or a modified IgG4 isotype with a kappa light chain framework. Additional substitutions L235E, or L235A/G237A (LAGA, as described in Int'l Pub. No. WO1998/006248) (numbering based upon the EU numbering system) were introduced to the Fc region to abrogate effector functions of the immunoglobulin component.

The association constants (k_a), dissociation constants (k_d), and equilibrium constants (K_D) of various anti-hPD-1 antibodies and anti-hPD-1 antibody-attenuated hIL-2 fusion proteins binding to recombinant human or cynomolgus PD-1 proteins was determined from the titration curves and the Carterra Kinetics software. The maximal feasible SPR signal generated (R_{max}) and residual standard deviation (Res SD) was also calculated. The results from the kinetics screen are summarized in Table 21, and demonstrated that the addition of the attenuated hIL-2 moiety on anti-hPD-1 antibodies did not modulate PD-1 antibody binding to the human PD-1 or cynomolgus PD-1 antigens. In a separate experiment, H7-632-hIgG1-LAGA (SEQ ID NOs: 414 and 415) was measured by SPR and had a steady state equilibrium dissociation constant (K_D) of 1.23×10^{-9} M and H7-767 had a $K_D = 1.93 \times 10^{-9}$ M.

TABLE 21

| Binding kinetics of anti-hPD-1 and anti-hPD-1-hIL-2 fusion proteins to recombinant human PD-1 and cynomolgus PD-1 by high-throughput SPR Carterra @ LSA™ | | | | | | | | | | | |
|--|--|--------------------------|-----------|----------|--------|---|--------------------------|-----------|----------|--------|-----|
| Kinetics Summary | | | | | | | | | | | |
| Human PD-1 | | | | | | Cyno PD-1 | | | | | |
| Name | k_a (M ⁻¹ s ⁻¹) | k_d (s ⁻¹) | K_D (M) | Rmax | Res SD | k_a (M ⁻¹ s ⁻¹) | k_d (s ⁻¹) | K_D (M) | Rmax | Res SD | |
| Anti-hPD-1 | 2H7-hIgG4-LE | 2.60E+05 | 8.20E-04 | 3.10E-09 | 146 | 8.5 | 1.40E+05 | 1.00E-03 | 7.10E-09 | 186 | 6.5 |
| | 2H7-hIgG4-LAGA | 1.70E+05 | 9.10E-04 | 5.30E-09 | 258 | 13 | 9.10E+04 | 1.10E-03 | 1.20E-08 | 295 | 11 |
| Anti-bodies | Abz1mod-hIgG4 | 1.40E+05 | 6.00E-05 | 4.26E-10 | 123 | 8.1 | 1.70E+05 | 6.20E-04 | 3.70E-09 | 183 | 10 |
| | A2-hIgG4 | 3.70E+04 | 1.30E-03 | 3.60E-08 | 341 | 7.8 | 6.80E+04 | 4.00E-02 | 5.89E-07 | 238 | 4.8 |
| | OMC.1.B6-hIgG4 | 7.70E+04 | 4.00E-03 | 5.20E-08 | 241 | 6.8 | 8.80E+04 | 4.40E-03 | 5.10E-08 | 262 | 5.5 |
| | OMC.2.C6-hIgG4 | 5.70E+04 | 6.60E-04 | 1.20E-08 | 229 | 8.7 | 5.50E+04 | 7.40E-04 | 1.30E-08 | 268 | 8.9 |
| | OMC.1.D6-hIgG4 | 4.10E+04 | 1.70E-03 | 4.20E-08 | 263 | 5.1 | 5.80E+04 | 4.00E-02 | 6.94E-07 | 182 | 4 |
| | OMC476pH7-hIgG4 | 6.00E+04 | 1.10E-03 | 1.80E-08 | 225 | 8.9 | 7.80E+04 | 1.70E-02 | 2.21E-07 | 254 | 2.8 |
| | OMC476pB11-hIgG4 | 5.00E+04 | 1.50E-03 | 3.00E-08 | 221 | 7 | 8.00E+04 | 2.60E-02 | 3.21E-07 | 204 | 2.7 |
| | OMC476pG10-hIgG4 | 9.30E+04 | 4.10E-03 | 4.40E-08 | 256 | 4.9 | 1.20E+05 | 6.00E-02 | 4.87E-07 | 188 | 4.9 |
| | OMC476pH10-hIgG4 | 1.00E+05 | 6.50E-03 | 6.40E-08 | 63 | 1.8 | 1.20E+05 | 5.90E-02 | 4.80E-07 | 81 | 3.8 |
| | OMC476pE4-hIgG4 | 7.90E+04 | 8.80E-04 | 1.10E-08 | 216 | 9.6 | 1.00E+05 | 3.50E-02 | 3.31E-07 | 204 | 6.3 |
| | D12-hIgG4 | 5.70E+04 | 4.60E-04 | 8.10E-09 | 234 | 9.9 | 5.90E+04 | 1.60E-02 | 2.72E-07 | 297 | 2.4 |
| | G12-hIgG4 | 5.30E+04 | 2.60E-03 | 5.00E-08 | 477 | 8.5 | 8.60E+04 | 6.50E-02 | 7.54E-07 | 327 | 7.8 |
| | EH12.2H7-mIgG1* | 1.10E+05 | 2.20E-03 | 1.90E-08 | 309 | 5.2 | 8.60E+04 | 7.30E-03 | 8.50E-08 | 307 | 4.2 |
| | J105-mIgG1* | 6.20E+04 | 5.30E-03 | 8.60E-08 | 186 | 2.8 | 5.00E+04 | 6.60E-02 | 1.30E-09 | 92 | 1.2 |
| | MIH4-mIgG1* | 1.30E+05 | 1.40E-03 | 1.00E-08 | 117 | 3.8 | 1.30E+05 | 1.20E-01 | 8.91E-07 | 61 | 1.8 |
| | J110-hIgG1 | 1.00E+05 | 1.00E-03 | 1.00E-08 | 346 | 15 | 4.10E+04 | 5.00E-02 | 1.20E-09 | 228 | 8.2 |
| | OPDIVO® (nivolumab) | 1.70E+05 | 1.70E-03 | 1.00E-08 | 55 | 2.6 | 1.50E+05 | 9.50E-04 | 6.40E-09 | 75 | 3.2 |
| KEYTRUDA® (pembrolizumab) | 2.90E+05 | 1.30E-03 | 4.50E-09 | 19 | 2.6 | 7.00E+05 | 4.00E-04 | 5.75E-07 | 53 | 3.7 | |
| Anti-hPD-1-attenuated hIL-2 | 2H7-hIgG1-LAGA-hIL-2 (T3A/D20A/R38E/C125A) | 1.50E+05 | 8.30E-04 | 5.40E-09 | 420 | 28 | 8.80E+04 | 9.70E-04 | 1.10E-08 | 502 | 21 |
| | 2H7-hIgG4-LE-hIL-2 (T3A/D20A/R38E/C125A) | 1.90E+05 | 8.10E-04 | 4.30E-09 | 374 | 17 | 9.00E+04 | 1.00E-03 | 1.10E-08 | 449 | 15 |
| Fusion Proteins | 2H7-hIgG4-LAGA-hIL-2 (T3A/D20A/R38E/C125A) | 1.70E+05 | 8.20E-04 | 4.80E-09 | 359 | 22 | 9.60E+04 | 9.80E-04 | 1.00E-08 | 429 | 17 |
| | 2H7-hIgG1-LAGA-hIL-2 (T3A/R38E/192K/C125A) | 1.80E+05 | 7.80E-04 | 4.30E-09 | 417 | 25 | 9.10E+04 | 9.70E-04 | 1.10E-08 | 505 | 19 |
| | hIgG4-LE-hIL-2 (T3A/R38E/192K/C125A) | 1.90E+05 | 8.80E-04 | 4.70E-09 | 380 | 19 | 9.50E+04 | 1.10E-03 | 1.20E-08 | 429 | 17 |
| | 2H7-hIgG4-LAGA-hIL-2 (T3A/R38E/192K/C125A) | 2.20E+05 | 8.20E-04 | 3.70E-09 | 355 | 17 | 1.00E+05 | 1.10E-03 | 1.10E-08 | 418 | 16 |
| | 2H7-hIgG1-LAGA-hIL-2 (T3A/R38E/D84K/C125A) | 1.30E+05 | 8.10E-04 | 6.20E-09 | 458 | 29 | 7.60E+04 | 1.00E-03 | 1.30E-08 | 532 | 23 |
| | 2H7-hIgG4-LE-hIL-2 (T3A/R38E/D84K/C125A) | 2.00E+05 | 9.40E-04 | 4.70E-09 | 232 | 13 | 1.30E+05 | 1.10E-03 | 8.20E-09 | 262 | 10 |
| | 2H7 hIgG4LAGA-df-hIL-2 (T3A/R38E/D84K/C125A) | 1.70E+05 | 7.30E-04 | 4.40E-09 | 400 | 20 | 8.10E+04 | 1.00E-03 | 1.30E-08 | 482 | 20 |

*Commercially sourced, no sequence available

Example 14: Determining Whether Anti-hPD-1 Antibodies and Anti-hPD-1-Attenuated hIL-2 Fusion Proteins Compete with Anti-hPD-1 #1 and Anti-hPD-1 #2 for Binding to PD-1 by Surface Plasmon Resonance (SPR)

Anti-hPD-1 and anti-hPD-1-attenuated hIL-2 fusion proteins were assayed for competition with one another using a sandwich method. Antibodies and corresponding antibody-IL-2 cytokine-fusion proteins were immobilized to HC30M chips using amine coupling chemistry described in Example 13. Following kinetic analysis described in Example 13, 80 nM human PD-1 (Acro Biosystems, Cat #PD-1-H5221-100 µg) was injected into the whole array. Competing anti-hPD-1 and anti-hPD-1-attenuated hIL-2 fusion proteins (analyte) were diluted to 30 µg/mL and subsequently injected into the array and binding parameters were assessed using SPR. Assessment of all anti-hPD-1 and anti-hPD-1-hIL-2 fusion proteins was performed in duplicate. Some variants tested had a modified human IgG1 or IgG4 kappa light chain framework with additional L235E or L235A/G237A (LAGA) substitutions to abrogate effector function of the immunoglobulin.

45 The screening of pairs of anti-hPD-1 or anti-hPD-1-attenuated hIL-2 fusion proteins allowed the identification of two bins, shown in Table 22. Antibodies and fusion proteins from Group 1 were able to bind hPD-1 in the presence of all antibodies and fusion proteins from Group 2, but competed with all members of the same Group. Antibodies and fusion proteins from Group 2 were able to bind hPD-1 in the presence of all antibodies and fusion proteins from Group 1, but competed with all members of the same Group. None of the anti-hPD-1 listed in Group 1 in Table 22 competed with KEYTRUDA® and OPDIVO®.

TABLE 22

| Groups 1 and 2 from anti-hPD-1 and anti-hPD-1-attenuated hIL-2 fusion protein binning screen by SPR | |
|---|------------------|
| Group 1 | Group 2 |
| Abz1mod-hIgG4 | KEYTRUDA® |
| OMC.1.B6-hIgG4 | OPDIVO® |
| OMC.1.D6-hIgG4 | Anti-hPD-1 clone |
| OMC.2.C6-hIgG4 | EH12.2H7-mIgG1* |
| OMC476pE4-hIgG4 | Anti-hPD-1 clone |

TABLE 22-continued

| Groups 1 and 2 from anti-hPD-1 and anti-hPD-1-attenuated hIL-2 fusion protein binning screen by SPR | |
|---|-------------|
| Group 1 | Group 2 |
| OMC476pH7-hIgG4 | J105-mIgG1* |
| OMC476pB11-hIgG4 | |
| OMC476pH10-hIgG4 | |
| OMC476pG10-hIgG4 | |
| A2-hIgG4 | |
| D12-hIgG4 | |
| G12-hIgG4 | |
| 2H7-hIgG4-LE | |
| 2H7-hIgG4-LE-df-hIL-2 | |
| (T3A/D20A/R38E/C125A) | |
| 2H7-hIgG4-LAGA-df-hIL-2 | |
| (T3A/D20A/R38E/C125A) | |
| 2H7-hIgG1-LAGA-df-hIL-2 | |
| (T3A/D20A/R38E/C125A) | |
| 2H7-hIgG4-LE-df-hIL-2 | |
| (T3A/R38E/I92K/C125A) | |
| 2H7-hIgG4-LAGA-df-hIL-2 | |
| (T3A/R38E/I92K/C125A) | |
| 2H7-hIgG1-LAGA-df-hIL-2 | |
| (T3A/R38E/I92K/C125A) | |
| 2H7-hIgG4-LE-df-hIL-2 | |
| (T3A/R38E/D84K/C125A) | |
| 2H7-hIgG4-LAGA-df-hIL-2 | |
| (T3A/R38E/D84K/C125A) | |
| 2H7-hIgG1-LAGA-df-hIL-2 | |
| (T3A/R38E/D84K/C125A) | |
| Anti-PD-1 clone MIH4 mIgG1 | |
| Anti-PD-1 clone J110 hIgG1 | |

*Commercially sourced, no sequence available

Example 15: Antagonism of Anti-hPD-1-Attenuated hIL-2 Fusion Proteins to hPD-1 in the Presence of Anti-hPD-1 #1 and Anti-hPD-1 #2

Anti-hPD-1-attenuated hIL-2 fusion proteins were tested for antagonism of hPD-1. Characterization of anti-hPD-1-attenuated hIL-2 fusion proteins was performed according to General Methods Protocol C. FIG. 7 illustrates these results. When compared to the PD-1 antagonists KEYTRUDA® or OPDIVO®, 2H7-hIgG4-df-hIL-2 (D20A/R38E), C51E6-5-hIgG4-L6-hIL-2 (D20A/R38E), and A2-hIgG4-df-hIL-2 (D20A/R38E) were non-antagonistic to human PD-1, as demonstrated by the low level of detectable luminescence. H7-632-hIgG1-LAGA and H7-767 were also tested for antagonist activity as described in General Protocol C. FIG. 15 illustrates that H7-632-hIgG1-LAGA and H7-767 do not block hPD-L1 (SEQ ID NO: 584) from interacting with the hPD-1 receptor.

For competition assays using the cell-based co-culture assay described in General protocol C, a few modifications were performed. Samples of the anti-hPD-1-attenuated hIL-2 fusion proteins were diluted to a fixed concentration of 400 nM and 20 μ L was added to 20 μ L of titrated anti-hPD-1 #1 or anti-hPD-1 #2. The 40 μ L mixture was added to CHO cells. Forty (40) μ L of Jurkat PD-1 effector cells were overlaid on the mixture of CHO cells and anti-hPD-1-attenuated hIL-2 fusion proteins. In this competition assay, a final concentration of saturating 100 nM anti-hPD-1-attenuated hIL-2 fusion proteins was tested in combination with titrated anti-hPD-1 #1 or anti-hPD-1 #2. The rest of the assay was performed as described in General Protocol C. FIG. 18A and FIG. 18B demonstrate that the addition of 100 nM anti-hPD-1-attenuated hIL-2 fusion proteins did not compete with the blocking of titrated anti-hPD-1 #1 binding to hPD-L1 (SEQ ID NO: 584).

Dose-titration curves of anti-hPD-1 #1 remained unchanged from curves without competitor antibody, suggesting that the presence of anti-hPD-1-attenuated hIL-2 fusion proteins did not compete with anti-hPD-1 #1 function even at high concentrations. In the presence of 100 nM 2H7-hIgG4-df-hIL-2 (D20A/R38E) and 100 nM C51E6-5-hIgG4-L6-hIL-2 (D20A/R38E), anti-hPD-1 #2 exhibited a 35% reduction in luminescence (RLU) at higher concentrations of anti-hPD-1 #2 (FIG. 18B) but it is unclear if this reduction was significant due to the extent of the standard deviation.

In the converse experiment, either anti-hPD-1 #1 or anti-hPD-1 #2 were diluted to a concentration of 400 nM and 20 μ L was combined with 20 μ L of titrated anti-hPD-1-attenuated hIL-2 fusion proteins. Anti-hPD-1-attenuated hIL-2 fusion proteins were serially titrated and the 40 μ L mixture was added to CHO cells, then overlaid with 40 μ L of Jurkat PD-1 Effector cells. The rest of the assay was performed as described in General Protocol C. FIG. 18C and FIG. 18D demonstrate that the addition of 100 nM anti-hPD-1 #1 (FIG. 18C) or 100 nM anti-hPD-1 #2 (FIG. 18D) do not impair the ability of the anti-hPD-1-attenuated hIL-2 fusion proteins to be antagonists. The observed flat curve above 18,000 relative luminescent units (RLU) indicated that there was no competition for antagonist activity and the anti-hPD-1-attenuated hIL-2 fusion proteins tested remained able to exhibit antagonist function even in the presence of anti-hPD-1 #1 or anti-hPD-1 #2.

Example 16: Testing Anti-hPD-1-Attenuated hIL-2 Fusion Proteins for Attenuation on the High-Affinity and Intermediate-Affinity hIL-2 Receptors with Cell-Based Proliferation Assays

Anti-hPD-1-attenuated hIL-2 fusion proteins were evaluated for the level of attenuation of hIL-2 activity using the cell proliferation assays on NK-92 and TF1+IL-2R β cell lines as described in General Protocol E. Control fusion proteins included fusion proteins incorporating an anti-DNase I antibody (designated 1H3) with a human IgG4 or human IgG1 backbone directly fused to hIL-2 or with a linker (SEQ ID NO: 355) to demonstrate the effects of non-targeting attenuated hIL-2 fusion proteins. The hIL-2 sequence of these constructs contained substitutions for attenuated hIL-2 activity as described in Example 2. Full, partial, or no agonistic IL-2 activity (inactive) was also assessed similarly to Example 3. Some of the variants tested were expressed on a modified human IgG1 or IgG4 isotype with a kappa light chain, with additional L235E or L235A/G237A (LAGA) substitutions in the Fc region to abrogate immunoglobulin effector function. In some antibody-cytokine fusion proteins, the hIL-2 cytokine was fused to the C-terminus of the light chain (LC fusion).

The calculated EC₅₀ of each antibody-cytokine fusion protein was determined from relative luminescence units (RLU), and fold change EC₅₀ was calculated when compared with recombinant human IL-2 (rhIL-2). The fold change from rhIL-2 and agonistic activity is summarized in Table 23. Agonistic activity was measured as full, partial, or inactive as determined by the maximal luminescence of antibody-attenuated hIL-2 fusion proteins in comparison to the maximal luminescence of rhIL-2. Antibody-attenuated hIL-2 fusion proteins dose-titration curves that reached the maximal luminescence as the rhIL-2 were considered to be variants with full activity. Partial activity was calculated as a percentage of full activity using rhIL-2 maximal luminescence as 100%. Maximal RLU of antibody-attenuated hIL-2

fusion proteins with less than 10% of the rhIL-2 maximal RLU at the highest concentration of 1200 nM were considered to have no agonist activity or inactive. For some

variants EC₅₀ values were estimated only since maximal luminescence was not reached, as annotated by an ^a in Table 23.

TABLE 23

| | | Fold change from rhIL-2 and agonistic activity of antibody-attenuated hIL-2 fusion proteins on NK-92 (high-affinity IL-2R) and TF1 + IL-2Rβ (intermediate-affinity IL-2R) cell lines. | | | |
|---|--|---|----------------------------|--|-----------------------------------|
| | Variants | Fold change from rhIL-2 (NK-92) | Agonistic Activity (NK-92) | Fold change from rhIL-2 (TF1 + IL-2Rβ) | Agonistic Activity (TF1 + IL-2Rβ) |
| Non-Targeted | 1H3-hIgG4-df-hIL-2 (WT) | 0 ^a | Full | 0-1 | Full |
| Antibody-Attenuated | 1H3-hIgG4-L6-hIL-2 (WT) | 0 ^a | Full | 0-1 | Full |
| hIL-2 Fusion | 1H3-hIgG4-df-hIL-2 (WT) LC fusion | 0 ^a | Full | 24 | Full |
| Proteins | 1H3-hIgG4-L6-hIL-2 (WT) LC fusion | 0 ^a | Full | 2 | Full |
| | 1H3-hIgG4-L6-hIL-2 (D20Y) | >10,000 on graph, NC ^a | Inactive | >10,000 on graph, NC ^a | Inactive |
| | 1H3-hIgG4-df-hIL-2 (D20Y) | >10,000 on graph, NC ^a | Partial, 60% | >10,000 on graph, NC ^a | Inactive |
| | 1H3-hIgG1-df-hIL-2 (D20Y) | 8539 ^a | Partial, 90% | >10,000 on graph, NC ^a | Inactive |
| | 1H3-hIgG4-L6-hIL-2 (D20A/R38P) | >10,000 ^a | Partial, 80% | 4132 ^a | Full |
| | 1H3-hIgG4-L6-hIL-2 (D20A/R38S) | >10,000 on graph, NC ^a | Partial, 90% | 9225 ^a | Full |
| | 1H3-hIgG4-L6-hIL-2 (D20A/R38D) | 118 ^a | Partial, 90% | 8591 ^a | Partial, 90% |
| | 1H3-hIgG4-L6-hIL-2 (D20A/R38Q/E95A) | 153 | Full | 5738 ^a | Full |
| | 1H3-hIgG4-L6-hIL-2 (D20A/F42H/E95A) | >10,000 ^a | Full | 1368 ^a | Full |
| | 1H3-hIgG4-L6-hIL-2 (R38D/I92D) | 190 | Full | 437 | Full |
| | 1H3-hIgG4-L6-hIL-2 (R38E/I92D) | 377 ^a | Full | 296 | Full |
| | 1H3-hIgG4-L6-hIL-2 (F42H/I92D) | 794 ^a | Full | 393 | Full |
| | 1H3-hIgG4-df-hIL-2 (D20A/R38E) | 868 ^a | Partial, 90%-Full | >10,000 ^a | Partial, 70%-Full |
| | 1H3-hIgG4-L6-hIL-2 (D20A/R38E) | 177 ^a | Partial, 60-80% | >10,000 ^a | Partial, 70%-Full |
| | 1H3-hIgG4-L6-hIL-2 (T3A/D20A/R38E) | >10,000 on graph, NC ^a | Partial, 40% | >10,000 | Partial, 70% |
| | 1H3-hIgG4-L6-hIL-2 (D20A/R38E/C125A) | >10,000 ^a | Partial, 20% | 6436 | Partial, 40% |
| | 1H3-hIgG4-L6-hIL-2 (T3A/D20A/R38E/C125A) | >10,000 on graph, NC ^a | Partial, 20% | >10,000 | Full |
| | 1H3-hIgG1-L6-hIL-2 (D20A/R38E) | NT | NT | 250-372 | Full |
| | 1H3-hIgG1-L6-hIL-2 (T3A/D20A/R38E) | 392 | Partial, 80% | 186 | Partial, 60% |
| | 1H3-hIgG1-L6-hIL-2 (D20A/R38E/C125A) | 2346 ^a | Partial, 80% | 2157 ^a | Partial, 60% |
| | 1H3-hIgG4-df-hIL-2 (D20A/R38E) LC fusion | >10,000 on graph, NC ^a | Inactive | >10,000 on graph, NC ^a | Inactive |
| | 1H3-hIgG4-L6-hIL-2 (D20A/R38E) LC fusion | >10,000 on graph, NC ^a | Inactive | 2155 ^a | Partial, 30% |
| | 1H3-hIgG1-L6-hIL2 (H16A) | 0 | Full | 0 ^a | Full |
| | 1H3-hIgG1-L6-hIL2 (F42A) | 0 | Full | 0 ^a | Full |
| | 1H3-hIgG1-L6-hIL2 (H16A/F42A) | 1 | Full | 0 ^a | Full |
| Anti-hPD-1-Attenuated hIL-2 Fusion Proteins | A2-hIgG4-df-hIL-2 (D20A/R38E) | 811 ^a | Partial, 20-90% | >10,000 ^a | Partial, 60-80% |
| | D12-hIgG4-df-hIL-2 (D20A/R38E) | >10,000 on graph, NC ^a | Partial, 20% | >10,000 ^a | Partial, 40% |
| | G12-hIgG4-df-hIL-2 (D20A/R38E) | >10,000 ^a | Partial, 20% | >10,000 ^a | Partial, 50% |
| | OMC476pB11-hIgG4-df-hIL-2 (D20A/R38E) | >10,000 on graph, NC ^a | Partial, 70% | 36 | Full |
| | OMC476pE4-hIgG4-df-hIL-2 (D20A/R38E) | >10,000 on graph, NC ^a | Partial, 70% | 1619 | Full |
| | OMC476pG10-hIgG4-df-hIL-2 (D20A/R38E) | >10,000 ^a | Partial, 70% | NC ^a | Inactive |
| | OMC476pH10-hIgG4-df-hIL-2 (D20A/R38E) | >10,000 on graph, NC ^a | Partial, 70% | 3563 ^a | Partial, 80% |
| | A2-hIgG4-df-hIL-2 (D20A/F42A) | 284 | Full | 4323 ^a | Partial, 80% |
| | A2-hIgG4-df-hIL-2 (D20A/F42S) | 3542 | Full | 4052 ^a | Partial, 90% |
| | A2-hIgG4-df-hIL-2 (D20S/R38E) | NT | NT | 7035 ^a | Full |
| | A2-hIgG4-df-hIL-2 (F42A/N88R) | 6423 | Full | 3757 ^a | Partial, 90% |
| | A2-hIgG4-df-hIL-2 (F42I/I92D) | 9543 | Full | 5611 ^a | Partial, 90% |
| | A2-hIgG4-df-hIL-2 (F42Q/I92D) | 8572 | Full | 3363 ^a | Full |
| | A2-hIgG4-df-hIL-2 (F42T/I92D) | 2175 | Full | 5649 ^a | Full |
| | A2-hIgG4-df-hIL-2 (F42W/I92D) | 1239 | Full | 4409 ^a | Partial, 50% |
| | A2-hIgG4-df-hIL-2 (R38E/D84K) | 160-1503 | Full | 1158-1716 | Partial, 90% |
| | A2-hIgG4-df-hIL-2 (R38E/I92K) | 252-977 | Full | 864-1655 | Partial, 80%-Full |
| | C51E6-5-hIgG4-df-hIL-2 (D20A/R38E) | 4317 | Partial, 70% | >10,000 ^a | Partial, 60% |
| | C51E6-5-hIgG4-L6-hIL-2 (D20A/R38E) | NT | NT | >10,000 ^a | Partial, 80% |

TABLE 23-continued

| Fold change from rhIL-2 and agonistic activity of antibody-attenuated hIL-2 fusion proteins on NK-92 (high-affinity IL-2R) and TF1 + IL-2Rβ (intermediate-affinity IL-2R) cell lines. | | | | |
|---|---------------------------------|----------------------------|--|-----------------------------------|
| Variants | Fold change from rhIL-2 (NK-92) | Agonistic Activity (NK-92) | Fold change from rhIL-2 (TF1 + IL-2Rβ) | Agonistic Activity (TF1 + IL-2Rβ) |
| C51E6-5-hIgG4-LE-df-hIL-2 (T3A/D20A/R38E/C125A) | 4326 | Partial, 80% | >10,000 ^a | Partial, 70% |
| C51E6-5-hIgG4-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) | 4336 | Partial, 60% | >10,000 on graph, NC ^a | Partial, 60% |
| OMC.1.B6-hIgG4-L6-hIL-2 (D20A/R38E) | NT | NT | 8460 ^a | Partial, 70% |
| OMC.1.D6-hIgG4-L6-hIL-2 (D20A/R38E) | NT | NT | >10,000 ^a | Partial, 70% |
| OMC.2.C6-hIgG4-L6-hIL-2 (D20A/R38E) | NT | NT | >10,000 ^a | Partial, 70% |
| 2A3.H7-hIgG4-df-hIL-2 (D20A/R38E) | NT | NT | 6603 ^a | Partial, 60% |
| 1H9-hIgG4-df-hIL-2 (D20A/R38E) | NT | NT | 9769 ^a | Partial, 90% |
| 1D5-hIgG4-df-hIL-2 (D20A/R38E) | NT | NT | 7420 ^a | Partial, 80% |
| 1D5-hIgG4-LE-df-hIL-2 (T3A/D20A/R38E/C125A) | NT | NT | NC ^a | Inactive |
| 1D5-hIgG4-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) | NT | NT | NC ^a | Partial, 20% |
| 2H7-hIgG1-df-hIL-2 (T3A/D20A/R38E/C125A) | 4839 ^a | Full | 2057 ^a | Full |
| 2H7-hIgG1-LE-df-hIL-2 (T3A/D20A/R38E/C125A) | 7727 ^a | Full | 6729 ^a | Partial, 80% |
| 2H7-hIgG1-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) | >10,000 ^a | Full | 3428 ^a | Partial, 50-60% |
| 2H7-hIgG4-df-hIL-2 (T3A/D20A/R38E/C125A) | 707-7206 ^a | Full | >10,000 ^a | Partial, 60%-Full |
| 2H7-hIgG4-LE-df-hIL-2 (T3A/D20A/R38E/C125A) | >10,000 | Full | >10,000 ^a | Partial, 50-60% |
| 2H7-hIgG4-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) | >10,000 | Full | 7480 ^a | Partial, 40-50% |
| H7-767 | >10,000 ^a | Partial, Full | >10,000 ^a | Full |
| 2H7-hIgG1-df-hIL-2 (T3A/R38E/D84K/C125A) | 1500 | Partial, 90% | 140 ^a | Full |
| 2H7-hIgG1-LE-df-hIL-2 (T3A/R38E/D84K/C125A) | 1268 | Partial, 90% | 517 ^a | Full |
| 2H7-hIgG1-LAGA-df-hIL-2 (T3A/R38E/D84K/C125A) | 2157-4035 | Partial, 90%-Full | 774-1650 ^a | Full |
| 2H7-hIgG4-df-hIL-2 (T3A/R38E/D84K/C125A) | 1602 | Partial, 90% | >10,000 ^a | Full |
| 2H7-hIgG4-LE-df-hIL-2 (T3A/R38E/D84K/C125A) | 1675-5096 | Partial, 90% | 1281-2842 ^a | Full |
| 2H7-hIgG4-LAGA-df-hIL-2 (T3A/R38E/D84K/C125A) | 1596-5689 | Partial, 90%-Full | 1203-3515 ^a | Partial, 60-80% |
| 2H7-hIgG1-df-hIL-2 (T3A/R38E/I92K/C125A) | 370 | Full | 160 | Full |
| 2H7-hIgG1-LE-df-hIL-2 (T3A/R38E/I92K/C125A) | 319 | Full | 656 | Full |
| 2H7-hIgG1-LAGA-df-hIL-2 (T3A/R38E/I92K/C125A) | 406-1280 | Full | 514-1569 ^a | Full |
| 2H7-hIgG4-df-hIL-2 (T3A/R38E/I92K/C125A) | 520 | Full | 789-926 | Partial, 80%-Full |
| 2H7-hIgG4-LE-df-hIL-2 (T3A/R38E/I92K/C125A) | 610-1675 | Full | 474-2080 ^a | Full |
| 2H7-hIgG4-LAGA-df-hIL-2 (T3A/R38E/I92K/C125A) | 827-2888 | Full | 737-2845 ^a | Partial, 70%-Full |
| 2H7-hIgG1-LAGA-df-hIL2 (T3A/D20S/R38E/C125A) | 6689 | Full | 9711 ^a | Partial, 70% |
| 2H7-hIgG1-LAGA-df-hIL2 (T3A/R38E/D84F/C125A) | 6199 | Full | 3915 | Full |
| 2H7-hIgG1-LAGA-df-hIL2 (T3A/R38E/192R/C125A) | 75 | Full | 89 | Full |
| 2H7-hIgG1-LAGA-df-hIL2 (T3A/R38E/192E/C125A) | 118 | Full | 53 | Full |
| 2H7-hIgG1-LAGA-df-hIL2 (T3A/R38E/192S/C125A) | 9 | Full | 30 | Full |
| 2H7-hIgG1-LAGA-df-hIL2 (T3A/R38E/192D/C125A) | 2717 | Full | 3396 ^a | Partial, 80% |
| 2H7-hIgG1-LAGA-df-hIL2 (T3A/H16E/R38E/C125A) | 126 | Full | 122 | Full |

NT = Not Tested

NC = Not Calculated by GraphPad Prism 7

^a = Fold change is an estimate only since a full four parameter logistic curve was not reached

Example 17: Rescue of IL-2 Activity of
Anti-hPD-1-Attenuated hIL-2 Fusion Proteins on a
Cell Line Expressing the Intermediate-Affinity
hIL-2 Receptor and hPD-1

Anti-hPD-1-attenuated hIL-2 fusion proteins were evaluated for rescue of hIL-2 activity using a targeted cell line expressing hPD-1. Briefly, the TF1+IL-2R β cell line described in General Methods Protocol D was modified through lentiviral transduction to express the hPD-1 receptor (SEQ ID NO: 580). Flow cytometry with a Brilliant Blue 515 conjugated hPD-1 antibody (BD Biosciences Cat #565936) was used to detect hPD-1 expressing TF1+IL-2R β cells. Cells were sorted for low hPD-1 expression (less than 10³ intensity on the Brilliant Blue 515 fluorophore). The pool was sorted twice more to collect cells that approximated hPD-1 expression levels on activated primary cells. This cell line (TF1+IL-2R β +hPD-1) was expanded and frozen in aliquots for the cell-based proliferation assays. Proliferation assays were performed as described in General Methods Protocol E with an incubation period of 3 days. Some variants tested had a modified human IgG1 or IgG4 kappa light chain framework with additional L235E or

L235A/G237A (LAGA) substitutions to abrogate effector function of the immunoglobulin.

Table 24 summarizes the results from the proliferation assays on the targeted TF1+IL-2R β +hPD-1 cell line. Agonistic activity was measured as full, partial, or inactive as determined by the maximal luminescence of antibody-attenuated hIL-2 fusion proteins in comparison to the maximal luminescence of rhIL-2. Antibody-attenuated hIL-2 fusion protein dose-titration curves that reached the maximal luminescence as the rhIL-2 were considered to be variants with full activity. Partial activity was calculated as a percentage of full activity using rhIL-2 maximal luminescence as 100%. Maximal RLU of antibody-attenuated hIL-2 fusion proteins with less than 10% of the rhIL-2 maximal RLU at the highest concentration of 1200 nM were considered to have no agonist activity or inactive. For some variants, EC₅₀ values were estimates only since a full curve was not reached. Many examples of anti-hPD-1-hIL-2 fusion proteins with attenuated hIL-2 showed rescued hIL-2 activity on the targeted cell line where the non-targeting antibody controls (denoted with 1H3) demonstrated no rescue of hIL-2 activity. Full rescue was illustrated by the reduction of fold-change from rhIL-2 to a value of 0 or 1.

TABLE 24

| Fold change from rhIL-2 and agonistic activity of antibody-hIL-2 fusion proteins on TF1 + IL-2R β + hPD-1 cell line (human PD-1 expressing cell line with intermediate-affinity IL-2R). | | | |
|---|---|--|-------------------|
| Variants | Fold decrease from rhIL-2 (TF1 + IL-2R β + hPD-1) | Agonistic Activity (TF1 + IL-2R β + hPD-1) | |
| Non-Targeted | 1H3-hIgG4-df-hIL-2 (WT) | 1 | Full |
| Antibody-Attenuated hIL-2 Fusion Proteins | 1H3-hIgG4-L6-hIL-2 (WT) | 1 | Full |
| | 1H3-hIgG4-L6-hIL-2 (D20Y) | NC ^a | Inactive |
| | 1H3-hIgG4-df-hIL-2 (D20Y) | NC ^a | Inactive |
| | 1H3-hIgG4-L6-hIL-2 (D20A/R38P) | 3074 ^a | Partial, 80% |
| | 1H3-hIgG4-L6-hIL-2 (D20A/R38S) | 4482 ^a | Partial, 80% |
| | 1H3-hIgG4-L6-hIL-2 (D20A/R38D) | 2964 ^a | Partial, 60% |
| | 1H3-hIgG4-L6-hIL-2 (D20A/R38Q/E95A) | 3538 ^a | Partial, 80% |
| | 1H3-hIgG4-L6-hIL-2 (D20A/F42H/E95A) | 657 ^a | Partial, 70% |
| | 1H3-hIgG4-L6-hIL-2 (R38D/I92D) | 1428 ^a | Full |
| | 1H3-hIgG4-L6-hIL-2 (R38E/I92D) | 1887 ^a | Full |
| | 1H3-hIgG4-L6-hIL-2 (F42H/I92D) | 2024 ^a | Full |
| | 1H3-hIgG4-df-hIL-2 (D20A/R38E) | 307-3628 ^a | Partial, 70%-Full |
| | 1H3-hIgG4-L6-hIL-2 (D20A/R38E) | 4883-5226 | Partial, 70%-Full |
| | 1H3-hIgG4-L6-hIL-2 (T3A/D20A/R38E) | 9167 ^a | Partial, 80% |
| | 1H3-hIgG4-L6-hIL-2 (D20A/R38E/C125A) | 4714 | Partial, 60% |
| | 1H3-hIgG4-L6-hIL-2 (T3A/D20A/R38E/C125A) | 4626 | Partial, 60% |
| | 1H3-hIgG1-L6-hIL-2 (D20A/R38E) | 297 | Full |
| | 1H3-hIgG1-L6-hIL-2 (T3A/D20A/R38E) | 513 | Partial, 80% |
| | 1H3-hIgG1-L6-hIL-2 (D20A/R38E/C125A) | 3342 | Partial, 80% |
| | 1H3-hIgG1-L6-hIL-2 (T3A/D20A/R38E/C125A) | 1081 | Partial, 90% |
| | 1H3-hIgG1-L6-hIL-2 (H16A) | 6459 | Full |
| | 1H3-hIgG1-L6-hIL-2 (F42A) | 4 ^a | Full |
| | 1H3-hIgG1-L6-hIL-2 (H16A/F42A) | 0 ^a | Full |
| | 1H3-hIgG1-L6-hIL-2 (D20T) | 2 ^a | Full |
| | 1H3-hIgG1-L6-hIL-2 (T3A/F42A/Y45A/L72G/C125A) | 75 ^a | Full |
| | | 2 ^a | Full |

TABLE 24-continued

| Fold change from rhIL-2 and agonistic activity of antibody-hIL-2 fusion proteins on TF1 + IL-2R β + hPD-1 cell line (human PD-1 expressing cell line with intermediate-affinity IL-2R). | | | |
|---|---|------------------|--|
| Variants | Fold decrease | | Agonistic Activity (TF1 + IL-2R β + hPD-1) |
| | from rhIL-2 (TF1 + IL-2R β + hPD-1) | | |
| Anti-hPD-1-Attenuated | A2-hIgG4-df-hIL-2 (D20A/R38E) | 0-1 ^a | Full |
| hIL-2 Fusion | D12-hIgG4-df-hIL-2 (D20A/R38E) | 1 ^a | Full |
| Proteins | G12-hIgG4-df-hIL-2 (D20A/R38E) | 1 ^a | Full |
| | OMC476pB11-hIgG4-df-hIL-2 (D20A/R38E) | 0 ^a | Full |
| | OMC476pE4-hIgG4-df-hIL-2 (D20A/R38E) | 2 ^a | Full |
| | OMC476pG10-hIgG4-df-hIL-2 (D20A/R38E) | 0 ^a | Full |
| | OMC476pH10-hIgG4-df-hIL-2 (D20A/R38E) | 1 ^a | Full |
| | A2-hIgG4-df-hIL-2 (D20A/F42A) | 2 ^a | Full |
| | A2-hIgG4-df-hIL-2 (D20A/F42S) | 1 ^a | Full |
| | A2-hIgG4-df-hIL-2 (D20S/R38E) | 0 ^a | Full |
| | A2-hIgG4-df-hIL-2 (F42A/N88R) | 0 ^a | Full |
| | A2-hIgG4-df-hIL-2 (F42I/I92D) | 9 ^a | Full |
| | A2-hIgG4-df-hIL-2 (F42Q/I92D) | 5 ^a | Full |
| | A2-hIgG4-df-hIL-2 (F42T/I92D) | 1 ^a | Full |
| | A2-hIgG4-df-hIL-2 (F42W/I92D) | 4 ^a | Full |
| | A2-hIgG4-df-hIL-2 (R38E/D84K) | 0-1 ^a | Full |
| | A2-hIgG4-df-hIL-2 (R38E/I92K) | 0-1 ^a | Full |
| | C51E6-5-hIgG4-df-hIL-2 (D20A/R38E) | 0-1 ^a | Partial, 70%-Full |
| | C51E6-5-hIgG4-L6-hIL-2 (D20A/R38E) | 1 ^a | Partial, 90% |
| | C51E6-5-hIgG4-LE-df-hIL-2 (T3A/D20A/R38E/C125A) | 1 ^a | Full |
| | C51E6-5-hIgG4-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) | 0 ^a | Full |
| | OMC.1.B6-hIgG4-L6-hIL-2 (D20A/R38E) | 0 ^a | Partial, 60% |
| | OMC.1.D6-hIgG4-L6-hIL-2 (D20A/R38E) | 0 ^a | Partial, 90% |
| | OMC.2.C6-hIgG4-L6-hIL-2 (D20A/R38E) | 0 ^a | Partial, 60% |
| | 2A3.H7-hIgG4-df-hIL-2 (D20A/R38E) | 0 ^a | Full |
| | 1H9-hIgG4-df-hIL-2 (D20A/R38E) | 0 ^a | Full |
| | 1D5-hIgG4-df-hIL-2 (D20A/R38E) | 1 ^a | Full |
| | 2H7-hIgG1-df-hIL-2 (T3A/D20A/R38E/C125A) | 1 ^a | Full |
| | 2H7-hIgG1-LE-df-hIL-2 (T3A/D20A/R38E/C125A) | 0 | Full |
| | 2H7-hIgG1-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) | 1 ^a | Full |
| | 2H7-hIgG4-df-hIL-2 (T3A/D20A/R38E/C125A) | 1 ^a | Full |
| | 2H7-hIgG4-LE-df-hIL-2 (T3A/D20A/R38E/C125A) | 1-4 ^a | Full |
| | 2H7-hIgG4-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) | 1 ^a | Full |
| | H7-767 | 0-1 ^a | Full |
| | 2H7-hIgG1-df-hIL-2 (T3A/R38E/D84K/C125A) | 2 ^a | Full |
| | 2H7-hIgG1-LE-df-hIL-2 (T3A/R38E/D84K/C125A) | 1 ^a | Full |
| | 2H7-hIgG1-LAGA-df-hIL-2 (T3A/R38E/D84K/C125A) | 1 ^a | Full |
| | 2H7-hIgG4-df-hIL-2 (T3A/R38E/D84K/C125A) | 1 ^a | Full |
| | 2H7-hIgG4-LE-df-hIL-2 (T3A/R38E/D84K/C125A) | 0-2 ^a | Full |
| | 2H7-hIgG4-LAGA-df-hIL-2 (T3A/R38E/D84K/C125A) | 1-3 ^a | Full |
| | 2H7-hIgG1-df-hIL-2 (T3A/R38E/I92K/C125A) | 1 ^a | Full |
| | 2H7-hIgG1-LE-df-hIL-2 (T3A/R38E/I92K/C125A) | 1 ^a | Full |
| | 2H7-hIgG1-LAGA-df-hIL-2 (T3A/R38E/I92K/C125A) | 1-2 ^a | Full |

TABLE 24-continued

| Fold change from rhIL-2 and agonistic activity of antibody-hIL-2 fusion proteins on TF1 + IL-2R β + hPD-1 cell line (human PD-1 expressing cell line with intermediate-affinity IL-2R). | | | |
|---|---|--|--|
| Variants | Fold decrease from rhIL-2 (TF1 + IL-2R β + hPD-1) | Agonistic Activity (TF1 + IL-2R β + hPD-1) | |
| 2H7-hIgG4-df-hIL-2 (T3A/R38E/I92K/C125A) | 1 ^a | Full | |
| 2H7-hIgG4-LE-df-hIL-2 (T3A/R38E/I92K/C125A) | 1 ^a | Full | |
| 2H7-hIgG4-LAGA-df-hIL-2 (T3A/R38E/I92K/C125A) | 1 ^a | Full | |
| 2H7-hIgG1-LAGA-df-hIL2 (T3A/D20S/R38E/C125A) | Not Attenuated on graph; NC ^a | Full | |
| 2H7-hIgG1-LAGA-df-hIL2 (T3A/R38E/D84F/C125A) | 0 ^a | Full | |
| 2H7-hIgG1-LAGA-df-hIL2 (T3A/R38E/I92R/C125A) | 0 ^a | Full | |
| 2H7-hIgG1-LAGA-df-hIL2 (T3A/R38E/I92E/C125A) | 2 ^a | Full | |
| 2H7-hIgG1-LAGA-df-hIL2 (T3A/R38E/I92S/C125A) | Not Attenuated on graph; NC ^a | Full | |
| 2H7-hIgG1-LAGA-df-hIL2 (T3A/R38E/C125A) | 0 ^a | Full | |
| 2H7-hIgG1-LAGA-df-hIL2 (T3A/H16E/R38E/C125A) | >10,000 ^a | Full | |

NC = Not Calculated by GraphPad Prism 7

^a = Fold change is an estimate only since a full four parameter logistic curve was not reached

Example 18: Evaluation of Surrogate Anti-hPD-1-Attenuated hIL-2 Fusion Proteins that Block or do not Block Mouse PD-L1 in an In Vivo Murine Colon Adenocarcinoma (MC38) Model

Since there are no accepted models to explore in vivo efficacy of oncology therapeutics in primates, a surrogate anti-mPD-1-attenuated hIL-2 fusion protein was generated and tested in a syngeneic murine tumor model. This MC38 colon adenocarcinoma model is routinely used to test efficacy of immuno-oncology therapeutics. To explore the in vivo effect of the anti-PD-1-attenuated hIL-2 fusion protein, a surrogate anti-mouse PD-1 antibody designated RMP1-14 (known to block mouse PD-L1 binding) and RMP1-30 (described as a mouse PD-L1 non-blocker) was fused to an attenuated hIL-2 at the C-terminus of the mouse IgG2b-N297A heavy chain and tested in an MC38 colon adenocarcinoma model. The hIL-2 moiety included the substitutions F42K, Y45R, and V69R that were tested on an IL-2 dependent mouse T lymphoblast cell line (CTLL-2) and that were demonstrated to be attenuated for mouse IL-2 activity. Human IL-2 can stimulate proliferation of mouse T cells at similar concentrations, however the same substitutions that attenuate activity on human IL-2 dependent cell lines do not attenuate activity on the CTLL-2 cell line (data not shown). As such, the F42K/Y45R/V69R substitutions were used in hIL-2 as a surrogate since they demonstrated attenuated IL-2 activity on mouse cell lines. Sequences comprising the heavy and light chain variable region sequences of anti-mouse PD-1 antibodies RMP1-14 and RMP1-30 (as described in Matsumoto K et al., J Immunol. 2004 Feb. 15; 172 (4): 2530-41) were also formatted onto a murine IgG2b-N297A background to generate anti-mPD-1 RMP1-14 mIgG2b-N297A (SEQ ID NOs: 564 and 566) and anti-mPD-1 RMP1-30 mIgG2b-N297A (SEQ ID NOs: 567 and 568). The mouse IgG2b isotype with an N297A substitution is the murine equivalent of an Fc isotype that abrogates Fc immune effector function. Surrogate antibodies and anti-

30 body-attenuated hIL-2 fusion proteins were produced, expressed and Protein-A purified using standard techniques.

In this murine tumor model, ten week old female C57BL/6NcrI (Charles River) mice were injected into the right flank with 5×10^5 MC38 colorectal carcinoma cells. When tumors reached 80-120 mm³, mice were sorted into cohorts (10 mice/group) and treatment began on day 1 of study. Anti-mPD-1 RMP1-14 mIgG2b-N297A, anti-mPD-1 RMP1-30 mIgG2b-N297A, anti-mPD-1 RMP1-14 mIgG2b-N297A-L6-hIL-2 (F42K/Y45R/V69R) (SEQ ID NOs: 565 and 566), and anti-mPD-1 RMP1-30 mIgG2b-N297A-L6-hIL-2 (F42K/Y45R/V69R) (SEQ ID NOs: 568 and 569) were dosed intraperitoneally at 5 mg/kg twice weekly for 4 weeks along with vehicle control (phosphate-buffered saline). Tumor size was measured with calipers twice weekly using the formula $(w^2 \times L)/2$ where w=width and L=length for the duration of the study. The study endpoint was a tumor volume of 1000 mm³ or survival at day 50, whichever came first.

FIG. 8 demonstrates that although the administration of anti-mPD-1 RMP1-14-mIgG2b-N297A or anti-mPD-1 RMP1-30-mIgG2b-N297A antibodies alone did not promote significant efficacy relative to treatment with vehicle control, the administration of anti-mPD-1 RMP1-14 mIgG2b-N297A-L6-hIL-2 (F42K/Y45R/V69R) or anti-mPD-1 RMP1-30 mIgG2b-N297A-L6-hIL-2 (F42K/Y45R/V69R) anti-PD-1-attenuated hIL-2 fusion proteins was associated with 90% and 100% complete tumor regressions respectively. These data demonstrate that the anti-tumor efficacy mediated by anti-mPD-1-hIL-2 (F42K/Y45R/V69R) fusion proteins does not require PD-1 checkpoint blockade and that efficacy is dependent on hIL-2 activity. The data further demonstrate that antibody mediated targeting of PD-1 expressing T cells is sufficient to promote potent anti-tumor efficacy in the MC38 tumor model.

Example 19: Surrogate Anti-hPD-1-Attenuated hIL-2 Fusion Protein Expands Effector Memory CD8+ T Cells in an In Vivo Murine Colon Adenocarcinoma Model

To understand the mechanism-of-action of the surrogate anti-hPD-1-attenuated hIL-2 fusion protein in vivo, a similar in vivo experiment to Example 18 was performed, followed by immunophenotyping of the resultant T cell populations in tumors, blood, spleens and lymph nodes after three doses. Ten week old female C57BL/6NCrI (Charles River) mice were subcutaneously implanted with the 5x10⁵ murine MC38 colon adenocarcinoma cancer tumor cells into the right flank and tumors were monitored for growth. Animals with tumors between 150-260 mm³ were divided between four groups with 10 mice per group for the study. After 21 days post-implantation, animals were dosed intraperitoneally with 0.2 mL/dose phosphate buffered saline (PBS) for the vehicle control, 5 mg/kg anti-KLH-C3-mIgG2b-N297A-L6-hIL-2 (F42K/Y45R/V69R), 5 mg/kg anti-mPD-1 RMP1-30 mIgG2b-N297A, or 5 mg/kg anti-mPD-1 RMP1-30 mIgG2b-N297A-L6-hIL-2 (F42K/Y45R/V69R) on days 1, 4 and 8. On day 9, tumors, spleens and inguinal lymph nodes were harvested from all mice and processed into single cell suspensions for subsequent flow cytometry analysis.

FIG. 9A charts the tumor volume growth (mm³) over 9 days from the first dose on day 1 where each point represents a mean of 10 mice. By day 8, anti-mPD-1 RMP1-30 mIgG2b-N297A-L6-hIL-2 (F42K/Y45R/V69R) had a reduction in tumor volume compared to other treatment groups. FIG. 9B summarizes the contribution of various CD8⁺ T cell subsets in the tumor of each treatment group in which T Central Memory were phenotyped as CD45⁺CD3⁺CD4⁻CD8⁺CD44⁺CD127⁺CD69⁻CD103⁻. T Effector Memory were CD45⁺CD3⁺CD4⁻CD8⁺CD44⁺CD127⁺CD69⁺CD103⁻CD62L⁻. T Resident Memory were CD45⁺CD3⁺CD4⁺CD8⁺CD44⁺CD127⁺CD69⁺CD103⁺, CD44⁺CD62L⁻ T cells were CD45⁺CD3⁺CD4⁻CD8⁺CD44⁺CD62L⁻ and T Naïve were CD45⁺CD3⁺CD4⁺CD8⁺CD44⁻CD62L⁺. In comparison to other treatment groups, there was expansion of the CD8⁺ T Effector Memory subset in the anti-mPD-1 RMP1-30 mIgG2b-N297A-L6-hIL-2 (F42K/Y45R/V69R) treated mice as indicated in the increase of the light grey slice of FIG. 9B. This was also illustrated in FIG. 9C in absolute counts (cells/μL) within the MC38 dissected tumor. Furthermore, within the tumor, there was a decrease in the absolute counts (cells/μL) of Regulatory T cells defined as expressing CD45⁺CD3⁺CD4⁺CD8⁺CD25⁺FoxP3⁺ markers.

The expansion of CD8⁺ T Effector Memory and decrease in Regulatory T cells has been associated with effective immunotherapy in both mice and humans.

Example 20: Anti-hPD-1-Attenuated hIL-2 Fusion Proteins are Active In Vivo in an NCG-PBMC Model

Engrafting human immune cells into NOD-Prkdc^{em2Cd52}IL-2rg^{em26Cd22}/NjuCrl (NCG) mice that lack functional T, B, and NK cells has been a valuable tool for evaluating efficacy of therapeutics hypothesized to stimulate human T cells. In this model, if the therapeutic activates human T cells, there would be a resulting expansion of T cells and accelerated graft-versus-host disease (GvHD).

Three independent donors for human peripheral mononuclear cell (hPBMC) engraftment were evaluated over a 4 week period for engraftment kinetics as well as expression

of human PD-1 and human IL-2 receptors on T cells. Of the three donors tested, the donor that induced the most T cells with an intermediate window for GvHD was chosen. 1.5x10⁷ hPBMCs were intravenously injected into NCG mice and divided into 8 groups of 8-16 mice. On days 7, 10, and 14, mice were intraperitoneally injected with three doses of 2H7-hlgG1-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) (SEQ ID NOs: 471, 425) (2.5 mg/kg, 5 mg/kg, or 10 mg/kg), 1H3-hlgG1-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) (SEQ ID NOs: 546, 374) (5 mg/kg or 10 mg/kg), 1H3-hlgG1-LAGA-df-hIL-2 (T3A/C125A) (SEQ ID NOs: 563, 374) (10 mg/kg), or 2H7-hlgG1-LAGA-df-hIL-2 (T3A/R38E/192K/C125A) (SEQ ID NOs: 474, 425) (5 mg/kg). The anti-DNase fusion protein both as a wild-type hIL-2 (1H3-hlgG1-LAGA-df-hIL-2 (T3A/C125A)) and with the attenuated hIL-2 moiety (1H3-hlgG1-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A)) was used as a non-targeting antibody control. Although the 1H3-hlgG1-LAGA-df-hIL-2 (T3A/C125A) fusion protein had no changes in the hIL-2 moiety which reduce hIL-2 activity, it did comprise the T3A and C125A substitutions to remove the predicted O-linked glycosylation site on human IL-2 (see for example Int'l Pub. No. WO2012/107417) and unpaired cysteine residue (see for example Int'l Pub. No. WO2018/184964), respectively. These substitutions have not demonstrated reduced hIL-2 potency in the clinic. On Day 21, blood, spleen, and lungs were harvested in which blood and spleens were processed for flow cytometry immunophenotyping while lungs were weighed.

After 21 days, flow cytometry immunophenotyping was performed on the blood and spleens of animals. Table 25 summarizes the markers used to delineate human T cell populations for subsequent analysis.

TABLE 25

Phenotypic markers to define human T cell subsets in NCG-PBMC mice

| Cell Population | Phenotypic Markers |
|----------------------|--|
| Pan T cells | CD3+ |
| CD8+ Naïve | CD3+CD4 ⁻ CD8+CD45RO ⁻ CCR7+ |
| CD8+ Effector | CD3+CD4 ⁻ CD8+CD45RO ⁺ CCR7 ⁻ |
| CD8+ Effector Memory | CD3+CD4 ⁻ CD8+CD45RO ⁺ CCR7 ⁻ |
| CD8+ Central Memory | CD3+CD4 ⁻ CD8+CD45RO ⁺ CCR7+ |
| CD4+ Naïve | CD3+CD4+CD8 ⁻ CD45RO ⁻ CCR7+ |
| CD4+ Effector | CD3+CD4+CD8 ⁻ CD45RO ⁺ CCR7 ⁻ |
| CD4+ Effector Memory | CD3+CD4+CD8 ⁻ CD45RO ⁺ CCR7 ⁻ |
| CD4+ Central Memory | CD3+CD4+CD8 ⁻ CD45RO ⁺ CCR7+ |
| Regulatory T cells | CD3+CD4+CD8 ⁻ CD25 ⁺ Foxp3+ |
| NK Cells | CD3 ⁻ CD56+ |

Body weight was measured for 21 days and normalized to day 1 for each individual animal as an assessment of graft-versus-host disease (GvHD) as illustrated in FIG. 10. Accelerated GvHD was observed in the 2H7-hlgG1-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) treated mice at 10 mg/kg. A small decrease in body weight was also observed in the 2H7-hlgG1-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) treated mice at 2.5 mg/kg, 5 mg/kg, and 2H7-hlgG1-LAGA-df-hIL-2 (T3A/R38E/192K/C125A) at 5 mg/kg. Although body weight loss was seen in the 1H3-hlgG1-LAGA-df-hIL-2 (T3A/C125A), it was not sustained.

The flow cytometry analysis correlated with the accelerated graft-versus-host disease (GvHD) observed. Using the phenotypic markers for human T cell subset delineation provided in Table 25, flow cytometry analysis of peripheral blood demonstrated only a minor expansion of CD3⁺, CD4⁺, and CD8⁺ T cell subsets (as quantified by a fold change from

vehicle control of between 10-fold to 50-fold for CD3⁺ T cells) in mice treated with 2H7-hIgG1-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) at 2.5 mg/kg and 5 mg/kg, and mice treated with 1H3-hIgG1-LAGA-df-hIL-2 (T3A/C125A) at 10 mg/kg. Furthermore, CD3⁺, CD4⁺, and CD8⁺ T cell subsets were greatly expanded (fold change from vehicle control was greater than 50-fold for CD3⁺ T cells) in the peripheral blood of mice treated with 2H7-hIgG1-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) at 10 mg/kg. Table 26 summarizes the expanded human T cell subsets.

TABLE 26

| Agent | Fold Change in numbers (Blood) | | |
|---|--------------------------------|--------------------------|--------------------------|
| | CD3 ⁺ T cells | CD4 ⁺ T cells | CD8 ⁺ T cells |
| Vehicle (PBS) | 1 | 1 | 1 |
| 1H3-hIgG1-LAGA-df-hIL-2 (T3A/C125A) 10 mg/kg | 22.76 | 27.73 | 16.13 |
| 1H3-hIgG1-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) 5 mg/kg | 1.94 | 2.12 | 1.74 |
| 1H3-hIgG1-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) 10 mg/kg | 0.56 | 0.56 | 0.57 |
| 2H7-hIgG1-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) 2.5 mg/kg | 24.57 | 32.4 | 14.4 |
| 2H7-hIgG1-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) 5 mg/kg | 53.03 | 70.74 | 22.86 |
| 2H7-hIgG1-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) 10 mg/kg | 203.3 | 296.94 | 58.82 |
| 2H7-hIgG1-LAGA-df-hIL-2 (T3A/R38E/I92K/C125A) 5 mg/kg | 31.79 | 48.76 | 8.79 |

N/A = Not Applicable

In addition to evaluating CD3⁺, CD4⁺, and CD8⁺ T cells between treatment groups, the memory and naïve subsets for CD4⁺ and CD8⁺ T cell subsets were also assessed. The phenotypic markers used for delineation of Naïve, Effector, Effector Memory and Central Memory for both CD4⁺ and CD8⁺ T cell is summarized in Table 25. There were no changes in Naïve, Effector or Central Memory T cells between treatment groups (data not shown). However, mice treated with 2H7-hIgG1-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) at 10 mg/kg had greatly expanded CD4⁺ and CD8⁺ Effector Memory (EM) T cells in the peripheral blood with an average cell number per milliliter greater than 5 million for CD8⁺ T cells and greater than 50 million for CD4⁺ T cells (FIGS. 11A and 11B). Box-and-whisker plots were graphed with the box around the first and third quartile, the horizontal line as the median, and lines indicated the minimum and maximum points. There was moderate expansion of CD8⁺ Effector Memory (EM) T cells defined as an average cell number per million between 1 to 5 million per milliliter for animals treated with 2H7-hIgG1-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) at 2.5 mg/kg and 5 mg/kg as well as for 1H3-hIgG1-LAGA-df-hIL-2 (T3A/C125A). There was moderate expansion of CD4⁺ Effector Memory (EM) T cells between 6 to 13 million per milliliter for CD4⁺ T cells in the mice treated with 2H7-hIgG1-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) at 2.5 mg/kg and 5 mg/kg.

In addition to stimulating effector T cells, IL-2 has been described to stimulate NK cells and regulatory T cells (Tregs) and since Tregs express high levels of CD25 and NK cells express CD122, these immune cell types were also evaluated. FIG. 12 illustrates that animals treated with 2H7-hIgG1-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) at the highest dose of 10 mg/kg did not expand human regulatory T cells and instead had the lowest percent of regulatory T cells (as phenotypically defined in Table 25) in the peripheral blood of animals. There was a dose-dependent decrease of human regulatory T cells and in comparison to vehicle control that had an average of 1.6% human CD3⁺ T cells that were Tregs, 2H7-hIgG1-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) at 10 mg/kg had an average of 0.16%

human CD3⁺ T cells that were Tregs. There were no changes in the percentage of human NK cells in peripheral blood (phenotype defined in Table 25) in all treatment groups in comparison to vehicle control (data not shown).

Example 21: Non-Clinical Safety Profile of Anti-hPD-1-Attenuated hIL-2 Fusion Proteins

Cynomolgus monkeys previously have been used to evaluate the toxicity of unmodified IL-2. Lethality was

observed in cynomolgus monkeys at exogenous recombinant IL-2 doses as low as 50 µg/kg/day. Since the binding of H7-767 to cynomolgus monkey hPD-1 on primary activated PBMCs was confirmed by flow cytometry (Example 12), a single-dose study for preliminary safety assessment was performed with both a variant of H7-767 (H7-02-hIgG1-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) (SEQ ID NOS: 582 and 583) and H7-767. H7-02-hIgG1-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) was delivered by 15 minute iv infusion to 8 monkeys at 1 mg/kg (4 animals) or 10 mg/kg (4 animals). Sampling at time-points up to 360 hours following infusion was performed. No adverse effects, gross toxicities, body weight loss, or lethality was observed (data not shown). A follow-up single-dose study using H7-767 was performed at higher doses of 5 mg/kg and 50 mg/kg similar to the first study, with sampling at time-points up to 360 hours post-infusion. Again, no adverse effects, gross toxicities, body weight loss or lethality was observed (data not shown).

Example 22: Attenuation of IL-2 Activity of Modified hIL-2 Proteins

The attenuation of IL-2 activity of modified hIL-2 proteins comprising a substitution at amino acid position 20 (D20) and a substitution at amino acid position 38 (R38) was tested in proliferation assays in both the NK-92 and TF1+IL-2Rβ cell lines as described in Example 5 above. The modified hIL-2 proteins were grouped into 7 groups (1 to 7) based upon the maximal agonist activity of the modified hIL-2 protein and the level of attenuation of potency on both the intermediate and high-affinity receptors (Table 27) relative to non-modified recombinant hIL-2. The criteria used for grouping the modified hIL-2 proteins was:

Group 1: Variants with the highest attenuation (i.e., >10,000-fold) and at least about 80% activity on the intermediate-affinity receptor but also had high attenuation and at least about 70% activity on the high-affinity receptor.

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Group 2: Variants with at least about 70% activity and >1,000-fold attenuation on the intermediate-affinity receptor, and about 20% activity to about 30% activity on the high-affinity receptor.

Group 3: Variants with about 50% activity to about 70% activity and >1,000-fold attenuation on the intermediate-affinity receptor, and about 20% activity on the high-affinity receptor.

Group 4: Variants with at least about 70% activity but only >500-fold attenuation on the intermediate-affinity receptor, and about 50% activity on the high-affinity receptor.

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Group 5: Variants with at least about 70% activity on both receptors but >10-fold to >300-fold attenuation on the intermediate-affinity receptor in descending order and 70-fold to 1500-fold attenuation on the high-affinity receptor also in descending order.

Group 6: Variants with only about 30% activity and >2,500-fold attenuation on the intermediate-affinity receptor, and no activity on the high-affinity receptor.

Group 7: Variants with no activity on both the intermediate-affinity receptor and high-affinity receptor.

TABLE 27

| Fold change from rhIL-2 and agonistic activity of modified hIL-2 proteins comprising a substitution at amino acid position 20 (D20) and a substitution at amino acid position 38 (R38) in a cell-based proliferation assay | | | | | | |
|--|--------------------------------|----------------------------|-----------------------------------|----------------------------|--|---|
| | Variants | SEQ ID NO of hIL-2 variant | Fold change from rhIL-2 (NK-92) | Agonistic Activity (NK-92) | Fold change from rhIL-2 (TF1 + IL-2R β) | Agonistic Activity (TF1 + IL-2R β) |
| Group 1 | 1H3-hIgG1-L6-hIL-2 (D20A/R38E) | 149 | 1183-2016 | at least about 70% | >10,000 ^a | at least about 80% |
| Group 2 | 1H3-hIgG1-L6-hIL-2 (D20Q/R38E) | 608 | >10,000 ^a | about 30% | 6665 | at least about 70% |
| Group 2 | 1H3-hIgG1-L6-hIL-2 (D20M/R38E) | 614 | >10,000 ^a | about 30% | 2607 | at least about 70% |
| Group 2 | 1H3-hIgG1-L6-hIL-2 (D20I/R38E) | 611 | >10,000 ^a | about 20% | 1782 | at least about 70% |
| Group 3 | 1H3-hIgG1-L6-hIL-2 (D20V/R38E) | 620 | >10,000 on graph, NC ^a | about 20% | 1849 | about 50% |
| Group 4 | 1H3-hIgG1-L6-hIL-2 (D20S/R38E) | 307 | >10,000 on graph, NC ^a | about 50% | 626 | at least about 70% |
| Group 5 | 1H3-hIgG1-L6-hIL-2 (D20N/R38E) | 607 | 1521 | at least about 70% | 378 | at least about 70% |
| Group 5 | 1H3-hIgG1-L6-hIL-2 (D20G/R38E) | 610 | 1288 | at least about 70% | 212 | at least about 70% |
| Group 5 | 1H3-hIgG1-L6-hIL-2 (D20T/R38E) | 617 | 524 | at least about 70% | 75 | at least about 70% |
| Group 5 | 1H3-hIgG1-L6-hIL-2 (D20E/R38E) | 609 | 77 | at least about 70% | 12 | at least about 70% |
| Group 6 | 1H3-hIgG1-L6-hIL-2 (D20H/R38E) | 306 | No activity | No activity | 2945 | about 30% |
| Group 7 | 1H3-hIgG1-L6-hIL-2 (D20L/R38E) | 612 | >10,000 ^a | No activity | >10,000 ^a | No activity |
| Group 7 | 1H3-hIgG1-L6-hIL-2 (D20K/R38E) | 613 | No activity | No activity | 544 | No activity |
| Group 7 | 1H3-hIgG1-L6-hIL-2 (D20F/R38E) | 615 | >10,000 ^a | No activity | >10,000 ^a | No activity |
| Group 7 | 1H3-hIgG1-L6-hIL-2 (D20P/R38E) | 616 | >10,000 ^a | No activity | >10,000 ^a | No activity |
| Group 7 | 1H3-hIgG1-L6-hIL-2 (D20W/R38E) | 618 | >10,000 ^a | No activity | >10,000 ^a | No activity |
| Group 7 | 1H3-hIgG1-L6-hIL-2 (D20Y/R38E) | 619 | >10,000 ^a | No activity | 1 | No activity |
| Group 7 | 1H3-hIgG1-L6-hIL-2 (D20R/R38E) | 606 | >10,000 ^a | No activity | >10,000 ^a | No activity |

Example 23: Activity of Surrogate Fusion Protein
in a Murine MC38 Colo-Rectal Tumor Model

Ten week old female C57BL/6NCrl mice were injected into the right flank with 5×10^5 syngeneic MC38 colorectal carcinoma cells. When tumors reached 80-120 mm³, mice were sorted into cohorts (10 mice/group) and treatment began on day 1 of study. All agents except hIL-2 were dosed intraperitoneally at 5 mg/kg twice weekly for 4 weeks, starting on day 1. hIL-2 was dosed intraperitoneally at 36,000 International Units once a day from days 1-5. Tumor size was measured with calipers twice weekly for the duration of the study. The study endpoint was a tumor volume of 1000 mm³ or survival at day 50 or progression free survival at day 70, whichever came first.

All test agents including antibody molecules and antibody-hIL-2 fusion proteins were generated using a mouse IgG2b Fc region with a single N297A amino-acid substitution at position 297, which prevents glycosylation of the Fc region and significantly reduces any Fc region-mediated immune effector function, thereby preventing cellular depletion in vivo. Anti-mPD-1 RMP1-14 is a monoclonal antibody antagonist of the mouse PD-1 receptor (Matsumoto, J Immunol 172:2530-2541, 2004). Anti-mPD-1 RMP1-14-hIL-2 F42K/Y45R/V69R is a bi-functional fusion protein consisting of the monoclonal RMP1-14 antibody antagonist of the mouse PD-1 receptor fused at its C-terminus via a flexible six amino-acid glycine/serine linker to hIL-2 F42K/Y45R/V69R (SEQ ID NO: 621) that is a reduced potency IL-2 variant. This molecule was designed to target a reduced potency hIL-2 variant directly to PD-1 expressing T cells in vivo in mice. Anti-KLH-hIL-2 F42K, Y45R, V69R is a control fusion protein consisting of an isotype control monoclonal antibody recognizing a non-mammalian antigen (key-hole limpet hemocyanin, KLH) fused at its C-terminus via a flexible six amino-acid glycine/serine linker to hIL-2 F42K, Y45R, V69R that is a reduced potency IL-2 variant.

Results are presented in FIG. 19. The MC38 colo-rectal tumor model is particularly responsive to antibody mediated PD-1 receptor inhibition. Although tumors growing in vehicle-treated mice rapidly reached study endpoint, 50% of mice treated with anti-mPD-1 RMP1-14 experienced complete tumor regression. In contrast, 100% of mice treated with an anti-mPD-1 RMP1-14-hIL-2 F42K, Y45R, V69R fusion protein experienced durable, long-term tumor regression. Mice treated with various combinations of the individual components of anti-mPD-1 RMP1-14-hIL-2 F42K,

Y45R, V69R fusion protein, including either anti-mPD-1 RMP1-14 combined with hIL-2 free cytokine (administered at a dose and regimen equivalent to a therapeutic dose in humans) or anti-mPD-1 RMP1-14 combined with a non-targeted anti-KLH-hIL-2 F42K, Y45R, V69R fusion protein did not recapitulate the efficacy seen with anti-mPD-1 RMP1-14-hIL-2 F42K, Y45R, V69R. These data demonstrate that targeting a reduced potency hIL-2 to PD-1 expressing cells significantly improves anti-tumor efficacy relative to an anti-PD-1 receptor antagonist and that the activity of the fusion protein is not due to the additive effects of the molecule's individual components.

Example 24: Evaluation of Protective Anti-Tumor
Immunity Induced by Surrogate Anti-mPD-1
RMP1-14-hIL-2 F42K, Y45R, V69R in the MC38
Colo-Rectal Tumor Model

Mice that had undergone a complete tumor regression in the primary tumor study described in Example 23 and that had survived to day 50 were subjected to a secondary tumor challenge without any additional drug therapy. For tumor re-challenge, mice were implanted on the left flank contralateral to the location of the primary tumor with 5×10^5 MC38 tumor cells. As a control group, 10 age-matched tumor naïve mice were also implanted with MC38 tumor cells.

FIG. 20 shows that all mice that had previously undergone a complete tumor regression in a prior primary tumor study and had survived to day 50 after treatment with anti-mPD-1 RMP1-14-hIL-2 F42K, Y45R, V69R were completely protected from secondary tumor development. In contrast, all tumor-naïve mice implanted with MC38 tumor cells went on to develop tumors that rapidly reached study endpoint of tumor volume of 100 mm³. The development of protective anti-tumor immunity in the absence of continued drug therapy suggests that anti-mPD-1 RMP1-14-hIL-2 F42K, Y45R, V69R induced an anti-tumor memory T cell response.

Those skilled in the art will appreciate that numerous changes and modifications can be made to the preferred embodiments disclosed herein and that such changes and modifications can be made without departing from the spirit of the invention. It is, therefore, intended that the appended claims cover all such equivalent variations as fall within the true spirit and scope of the invention.

The disclosures of each patent, patent application, and publication cited or described in this document are hereby incorporated herein by reference, in its entirety.

TABLE 28

| Exemplary Antibodies | | |
|-----------------------------------|--|--|
| Antibody Name | Heavy chain | Light chain |
| Anti-hPD-1 #1-mIgG2b-N297A | Anti-hPD-1 #1-mIgG2b-N297A HC (SEQ ID NO: 348) | Anti-hPD-1 #1-mKappa LC (SEQ ID NO: 349) |
| Anti-hPD-1 #2-mIgG2b-N297A | Anti-hPD-1 #2-mIgG2b-N297A HC (SEQ ID NO: 350) | Anti-hPD-1 #2-mKappa LC (SEQ ID NO: 351) |
| hIL-2 Nterm light chain df | 1H3-hIgG1 HC (SEQ ID NO: 379) | hIL-2-df-1H3-hkappa LC (SEQ ID NO: 356) |
| hIL-2 Nterm light chain L6 fusion | 1H3-hIgG1 HC (SEQ ID NO: 379) | hIL-2-L6-1H3-hkappa LC (SEQ ID NO: 357) |
| hIL-2 Nterm heavy chain df | hIL-2-df-1H3-hIgG1 HC (SEQ ID NO: 358) | 1H3-hKappa LC (SEQ ID NO: 374) |
| hIL-2 Nterm heavy chain L6 fusion | hIL-2-L6-1H3-hIgG1 HC (SEQ ID NO: 359) | 1H3-hKappa LC (SEQ ID NO: 374) |
| hIL-2 Cterm heavy chain df | 1H3-hIgG1-df-hIL-2 HC (SEQ ID NO: 360) | 1H3-hKappa LC (SEQ ID NO: 374) |
| hIL-2 Cterm heavy chain L6 fusion | 1H3-hIgG1-L6-hIL-2 HC (SEQ ID NO: 361) | 1H3-hKappa LC (SEQ ID NO: 374) |

TABLE 28-continued

| Exemplary Antibodies | | |
|---|---|---|
| Antibody Name | Heavy chain | Light chain |
| hIL-2 Cterm light chain df | 1H3-hIgG1 HC (SEQ ID NO: 379) | 1H3-hKappa-df-hIL-2 (WT) LC (SEQ ID NO: 362) |
| hIL-2 Cterm light chain L6 fusion | 1H3-hIgG1 HC (SEQ ID NO: 379) | 1H3-hKappa-L6-hIL-2 (WT) LC (SEQ ID NO: 363) |
| hCD25-L20-hIL-2 Nterm heavy chain df | hCD25-L20-hIL-2-df-1H3-hIgG1 HC (SEQ ID NO: 365) | 1H3-hKappa LC (SEQ ID NO: 374) |
| hCD25-L20-hIL-2 Nterm heavy chain L6 fusion | hCD25-L20-hIL-2-L6-1H3-hIgG1 HC (SEQ ID NO: 366) | 1H3-hKappa LC (SEQ ID NO: 374) |
| hCD25-L20-hIL-2 Nterm light chain df | 1H3-hIgG1 HC (SEQ ID NO: 379) | hCD25-L20-hIL-2-df-1H3-hKappa LC (SEQ ID NO: 367) |
| hCD25-L20-hIL-2 Nterm light chain L6 fusion | 1H3-hIgG1 HC (SEQ ID NO: 379) | hCD25-L20-hIL-2-L6-1H3-hKappa LC (SEQ ID NO: 368) |
| hCD25-L20-hIL-2 Cterm heavy chain df | 1H3-hIgG1-df-hCD25-L20-hIL-2 HC (SEQ ID NO: 369) | 1H3-hKappa LC (SEQ ID NO: 374) |
| hCD25-L20-hIL-2 Cterm heavy chain L6 fusion | 1H3-hIgG1-L6-hCD25-L20-hIL-2 HC (SEQ ID NO: 370) | 1H3-hKappa LC (SEQ ID NO: 374) |
| hCD25-L20-hIL-2 Cterm light chain df | 1H3-hIgG1 HC (SEQ ID NO: 379) | 1H3-hKappa-df-hCD25-L20-hIL-2 LC (SEQ ID NO: 371) |
| hCD25-L20-hIL-2 Cterm light chain L6 fusion | 1H3-hIgG1 HC (SEQ ID NO: 379) | 1H3-hKappa-L6-hCD25-L20-hIL-2 LC (SEQ ID NO: 372) |
| 2D12-mIgG1-D265A-L6-hIL-2 | 2D12-mIgG1-D265A-L6-hIL-2 HC (SEQ ID NO: 375) | 2D12-mKappa LC (SEQ ID NO: 376) |
| 2H7-hIgG4 | 2H7-hIgG4 HC (SEQ ID NO: 424) | 2H7-hKappa LC (SEQ ID NO: 425) |
| C51E6-5-hIgG4 | C51E6-5-hIgG4 HC (SEQ ID NO: 426) | C51E6-5-hKappa LC (SEQ ID NO: 427) |
| A2-hIgG4 | A2-hIgG4 HC (SEQ ID NO: 428) | A2-hLambda LC (SEQ ID NO: 429) |
| H7-632-hIgG1-LAGA | H7-632 HC (SEQ ID NO: 414) | H7-632 LC (SEQ ID NO: 415) |
| 2H7-hIgG4-df-hIL-2 (D20A/R38E) | 2H7-hIgG4-df-hIL-2 (D20A/R38E) HC (SEQ ID NO: 430) | 2H7-hKappa LC (SEQ ID NO: 425) |
| C51E6-5-hIgG4-L6-hIL-2 (D20A/R38E) | C51E6-5-hIgG4-L6-hIL-2 (D20A/R38E) HC (SEQ ID NO: 432) | C51E6-5-hKappa LC (SEQ ID NO: 427) |
| A2-hIgG4-df-hIL-2 (D20A/R38E) | A2-hIgG4-df-hIL-2 (D20A/R38E) HC (SEQ ID NO: 433) | A2-hLambda LC (SEQ ID NO: 429) |
| 1H3-hIgG4-df-hIL-2 (D20A/R38E) | 1H3-hIgG4-df-hIL-2 (D20A/R38E) HC (SEQ ID NO: 434) | 1H3-hKappa LC (SEQ ID NO: 374) |
| 2H7-hIgG4-df-hIL-2 (T3A/D20A/R38E/C125A) | 2H7-hIgG4-df-hIL-2 (T3A/D20A/R38E/C125A) HC (SEQ ID NO: 435) | 2H7-hKappa LC (SEQ ID NO: 425) |
| OMC.1.B6-hIgG4 | OMC.1.B6-hIgG4 HC (SEQ ID NO: 438) | OMC.1.B6-hLambda LC (SEQ ID NO: 439) |
| OMC.2.C6-hIgG4 | OMC.2.C6-hIgG4 HC (SEQ ID NO: 440) | OMC.2.C6-hLambda LC (SEQ ID NO: 441) |
| OMC.1.D6-hIgG4 | OMC.1.D6-hIgG4 HC (SEQ ID NO: 442) | OMC.1.D6-hLambda LC (SEQ ID NO: 443) |
| D12-hIgG4 | D12-hIgG4 HC (SEQ ID NO: 444) | D12-hLambda LC (SEQ ID NO: 445) |
| G12-hIgG4 | G12-hIgG4 HC (SEQ ID NO: 446) | G12-hLambda LC (SEQ ID NO: 447) |
| Abz1mod-hIgG4 | Abz1mod-hIgG4 HC (SEQ ID NO: 449) | Abz1mod-hKappa LC (SEQ ID NO: 450) |
| Anti-hPD-1 #1-hIgG4-L6-hIL-2 (D20A/R38E) | Anti-hPD-1 #1-hIgG4-L6-hIL-2 (D20A/R38E) (SEQ ID NO: 451) | Anti-hPD-1 #1-hKappa (SEQ ID NO: 452) |
| OMC.1.B6-hIgG4-L6-hIL-2 (D20A/R38E) | OMC.1.B6-hIgG4-L6-hIL-2 (D20A/R38E) HC (SEQ ID NO: 453) | OMC.1.B6-hLambda LC (SEQ ID NO: 439) |
| OMC.2.C6-hIgG4-L6-hIL-2 (D20A/R38E) | OMC.2.C6-hIgG4-L6-hIL-2 (D20A/R38E) HC (SEQ ID NO: 454) | OMC.2.C6-hLambda LC (SEQ ID NO: 441) |
| OMC.1.D6-hIgG4-L6-hIL-2 (D20A/R38E) | OMC.1.D6-hIgG4-L6-hIL-2 (D20A/R38E) HC (SEQ ID NO: 455) | OMC.1.D6-hLambda LC (SEQ ID NO: 443) |
| D12-hIgG4-df-hIL-2 (D20A/R38E) | D12-hIgG4-df-hIL-2 (D20A/R38E) HC (SEQ ID NO: 456) | D12-hLambda LC (SEQ ID NO: 445) |
| G12-hIgG4-df-hIL-2 (D20A/R38E) | G12-hIgG4-df-hIL-2 (D20A/R38E) HC (SEQ ID NO: 457) | G12-hLambda LC (SEQ ID NO: 447) |
| 2H7-hIgG4-LE | 2H7-hIgG4-LE HC (SEQ ID NO: 458) | 2H7-hKappa LC (SEQ ID NO: 425) |
| 2H7-hIgG4-LAGA | 2H7-hIgG4-LAGA HC (SEQ ID NO: 459) | 2H7-hKappa LC (SEQ ID NO: 425) |
| OMC476pH7-hIgG4 | OMC476pH7-hIgG4 HC (SEQ ID NO: 461) | OMC476pB11.H7 LC (SEQ ID NO: 462) |
| OMC476pB11-hIgG4 | OMC476pB11-hIgG4 HC (SEQ ID NO: 463) | OMC476pB11.H7 LC (SEQ ID NO: 462) |
| OMC476pG10-hIgG4 | OMC476pG10-hIgG4 HC (SEQ ID NO: 464) | OMC476pG10.H10 LC (SEQ ID NO: 466) |
| OMC476pH10-hIgG4 | OMC476pH10-hIgG4 HC (SEQ ID NO: 465) | OMC476pG10.H10 LC (SEQ ID NO: 466) |
| OMC476pE4-hIgG4 | OMC476pE4-hIgG4 HC (SEQ ID NO: 467) | OMC476pE4 LC (SEQ ID NO: 468) |
| J110-hIgG1 | J110-hIgG1 HC (SEQ ID NO: 469) | J110-hKappa LC (SEQ ID NO: 470) |
| 2H7-hIgG1-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) | 2H7-hIgG1-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) HC (SEQ ID NO: 471) | 2H7-hKappa LC (SEQ ID NO: 425) |

TABLE 28-continued

| Exemplary Antibodies | | |
|--|--|---|
| Antibody Name | Heavy chain | Light chain |
| 2H7-hIgG4-LE-df-hIL-2 (T3A/D20A/R38E/C125A) | 2H7-hIgG4-LE-df-hIL-2 (T3A/D20A/R38E/C125A) HC (SEQ ID NO: 472) | 2H7-hKappa LC (SEQ ID NO: 425) |
| 2H7-hIgG4-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) | 2H7-hIgG4-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) HC (SEQ ID NO: 473) | 2H7-hKappa LC (SEQ ID NO: 425) |
| 2H7-hIgG1-LAGA-df-hIL-2 (T3A/R38E/I92K/C125A) | 2H7-hIgG1-LAGA-df-hIL-2 (T3A/R38E/I92K/C125A) HC (SEQ ID NO: 474) | 2H7-hKappa LC (SEQ ID NO: 425) |
| hIgG4-LE-df-hIL-2 (T3A/R38E/I92K/C125A) | hIgG4-LE-df-hIL-2 (T3A/R38E/I92K/C125A) HC (SEQ ID NO: 475) | 2H7-hKappa LC (SEQ ID NO: 425) |
| 2H7-hIgG4-LAGA-df-hIL-2 (T3A/R38E/I92K/C125A) | 2H7-hIgG4-LAGA-df-hIL-2 (T3A/R38E/I92K/C125A) HC (SEQ ID NO: 476) | 2H7-hKappa LC (SEQ ID NO: 425) |
| 2H7-hIgG1-LAGA-df-hIL-2 (T3A/R38E/D84K/C125A) | 2H7-hIgG1-LAGA-df-hIL-2 (T3A/R38E/D84K/C125A) HC (SEQ ID NO: 477) | 2H7-hKappa LC (SEQ ID NO: 425) |
| 2H7-hIgG4-LE-df-hIL-2 (T3A/R38E/D84K/C125A) | 2H7-hIgG4-LE-df-hIL-2 (T3A/R38E/D84K/C125A) HC (SEQ ID NO: 478) | 2H7-hKappa LC (SEQ ID NO: 425) |
| 2H7-hIgG4-LAGA-df-hIL-2 (T3A/R38E/D84K/C125A) | 2H7-hIgG4-LAGA-df-hIL-2 (T3A/R38E/D84K/C125A) HC (SEQ ID NO: 479) | 2H7-hKappa LC (SEQ ID NO: 425) |
| 1H3-hIgG4-df-hIL-2 (WT) | 1H3-hIgG4-df-hIL-2 (WT) HC (SEQ ID NO: 480) | 1H3-hKappa LC (SEQ ID NO: 374) |
| 1H3-hIgG4-L6-hIL-2 (WT) | 1H3-hIgG4-L6-hIL-2 (WT) HC (SEQ ID NO: 481) | 1H3-hKappa LC (SEQ ID NO: 374) |
| 1H3-hIgG4-df-hIL-2 (WT) LC fusion | 1H3-hIgG4 HC (SEQ ID NO: 482) | 1H3-hKappa-df-hIL-2 (WT) LC (SEQ ID NO: 362) |
| 1H3-hIgG4-L6-hIL-2 (WT) LC fusion | 1H3-hIgG4 HC (SEQ ID NO: 482) | 1H3-hKappa-L6-hIL-2 (WT) LC (SEQ ID NO: 363) |
| 1H3-hIgG4-L6-hIL-2 (D20Y) | 1H3-hIgG4-L6-hIL-2 (D20Y) HC (SEQ ID NO: 485) | 1H3-hKappa LC (SEQ ID NO: 374) |
| 1H3-hIgG4-df-hIL-2 (D20Y) | 1H3-hIgG4-df-hIL-2 (D20Y) HC (SEQ ID NO: 486) | 1H3-hKappa LC (SEQ ID NO: 374) |
| 1H3-hIgG1-df-hIL-2 (D20Y) | 1H3-hIgG1-df-hIL-2 (D20Y) HC (SEQ ID NO: 487) | 1H3-hKappa LC (SEQ ID NO: 374) |
| 1H3-hIgG4-L6-hIL-2 (D20A/R38P) | 1H3-hIgG4-L6-hIL-2 (D20A/R38P) HC (SEQ ID NO: 488) | 1H3-hKappa LC (SEQ ID NO: 374) |
| 1H3-hIgG4-L6-hIL-2 (D20A/R38S) | 1H3-hIgG4-L6-hIL-2 (D20A/R38S) HC (SEQ ID NO: 489) | 1H3-hKappa LC (SEQ ID NO: 374) |
| 1H3-hIgG4-L6-hIL-2 (D20A/R38D) | 1H3-hIgG4-L6-hIL-2 (D20A/R38D) HC (SEQ ID NO: 490) | 1H3-hKappa LC (SEQ ID NO: 374) |
| 1H3-hIgG4-L6-hIL-2 (D20A/R38Q/E95A) | 1H3-hIgG4-L6-hIL-2 (D20A/R38Q/E95A) HC (SEQ ID NO: 491) | 1H3-hKappa LC (SEQ ID NO: 374) |
| 1H3-hIgG4-L6-hIL-2 (D20A/F42H/E95A) | 1H3-hIgG4-L6-hIL-2 (D20A/F42H/E95A) HC (SEQ ID NO: 492) | 1H3-hKappa LC (SEQ ID NO: 374) |
| 1H3-hIgG4-L6-hIL-2 (R38D/I92D) | 1H3-hIgG4-L6-hIL-2 (R38D/I92D) HC (SEQ ID NO: 493) | 1H3-hKappa LC (SEQ ID NO: 374) |
| 1H3-hIgG4-L6-hIL-2 (R38E/I92D) | 1H3-hIgG4-L6-hIL-2 (R38E/I92D) HC (SEQ ID NO: 494) | 1H3-hKappa LC (SEQ ID NO: 374) |
| 1H3-hIgG4-L6-hIL-2 (F42H/I92D) | 1H3-hIgG4-L6-hIL-2 (F42H/I92D) HC (SEQ ID NO: 495) | 1H3-hKappa LC (SEQ ID NO: 374) |
| 1H3-hIgG4-L6-hIL-2 (D20A/R38E) | 1H3-hIgG4-L6-hIL-2 (D20A/R38E) HC (SEQ ID NO: 496) | 1H3-hKappa LC (SEQ ID NO: 374) |
| 1H3-hIgG4-L6-hIL-2 (T3A/D20A/R38E) | 1H3-hIgG4-L6-hIL-2 (T3A/D20A/R38E) HC (SEQ ID NO: 497) | 1H3-hKappa LC (SEQ ID NO: 374) |
| 1H3-hIgG4-L6-hIL-2 (D20A/R38E/C125A) | 1H3-hIgG4-L6-hIL-2 (D20A/R38E/C125A) HC (SEQ ID NO: 498) | 1H3-hKappa LC (SEQ ID NO: 374) |
| 1H3-hIgG4-L6-hIL-2 (T3A/D20A/R38E/C125A) | 1H3-hIgG4-L6-hIL-2 (T3A/D20A/R38E/C125A) HC (SEQ ID NO: 499) | 1H3-hKappa LC (SEQ ID NO: 374) |
| 1H3-hIgG1-L6-hIL-2 (D20A/R38E) | 1H3-hIgG1-L6-hIL-2 (D20A/R38E) HC (SEQ ID NO: 500) | 1H3-hKappa LC (SEQ ID NO: 374) |
| 1H3-hIgG1-L6-hIL-2 (T3A/D20A/R38E) | 1H3-hIgG1-L6-hIL-2 (T3A/D20A/R38E) HC (SEQ ID NO: 501) | 1H3-hKappa LC (SEQ ID NO: 374) |
| 1H3-hIgG1-L6-hIL-2 (D20A/R38E/C125A) | 1H3-hIgG1-L6-hIL-2 (D20A/R38E/C125A) HC (SEQ ID NO: 502) | 1H3-hKappa LC (SEQ ID NO: 374) |
| 1H3-hIgG4-df-hIL-2 (D20A/R38E) LC fusion | 1H3-hIgG4 HC (SEQ ID NO: 482) | 1H3-hKappa-df-hIL-2 (D20A/R38E) LC (SEQ ID NO: 503) |

TABLE 28-continued

| Exemplary Antibodies | | |
|---|---|---|
| Antibody Name | Heavy chain | Light chain |
| 1H3-hIgG4-L6-hIL-2 (D20A/R38E) LC fusion | 1H3-hIgG4 HC (SEQ ID NO: 482) | 1H3-hKappa-L6-hIL-2 (D20A/R38E) LC (SEQ ID NO: 504) |
| OMC476pB11-hIgG4-df-hIL-2 (D20A/R38E) | OMC476pB11-hIgG4-df-hIL-2 (D20A/R38E) HC (SEQ ID NO: 505) | OMC476pB11.H7 LC (SEQ ID NO: 462) |
| OMC476pE4-hIgG4-df-hIL-2 (D20A/R38E) | OMC476pE4-hIgG4-df-hIL-2 (D20A/R38E) HC (SEQ ID NO: 506) | OMC476pE4 LC (SEQ ID NO: 468) |
| OMC476pG10-hIgG4-df-hIL-2 (D20A/R38E) | OMC476pG10-hIgG4-df-hIL-2 (D20A/R38E) HC (SEQ ID NO: 507) | OMC476pG10.H10 LC (SEQ ID NO: 466) |
| OMC476pH10-hIgG4-df-hIL-2 (D20A/R38E) | OMC476pH10-hIgG4-df-hIL-2 (D20A/R38E) HC (SEQ ID NO: 508) | OMC476pG10.H10 LC (SEQ ID NO: 466) |
| A2-hIgG4-df-hIL-2 (D20A/F42A) | A2-hIgG4-df-hIL-2 (D20A/F42A) HC (SEQ ID NO: 509) | A2-hLambda LC (SEQ ID NO: 429) |
| A2-hIgG4-df-hIL-2 (D20A/F42S) | A2-hIgG4-df-hIL-2 (D20A/F42S) HC (SEQ ID NO: 510) | A2-hLambda LC (SEQ ID NO: 429) |
| A2-hIgG4-df-hIL-2 (D20S/R38E) | A2-hIgG4-df-hIL-2 (D20S/R38E) HC (SEQ ID NO: 511) | A2-hLambda LC (SEQ ID NO: 429) |
| A2-hIgG4-df-hIL-2 (F42A/N88R) | A2-hIgG4-df-hIL-2 (F42A/N88R) HC (SEQ ID NO: 512) | A2-hLambda LC (SEQ ID NO: 429) |
| A2-hIgG4-df-hIL-2 (F42I/I92D) | A2-hIgG4-df-hIL-2 (F42I/I92D) HC (SEQ ID NO: 513) | A2-hLambda LC (SEQ ID NO: 429) |
| A2-hIgG4-df-hIL-2 (F42Q/I92D) | A2-hIgG4-df-hIL-2 (F42Q/I92D) HC (SEQ ID NO: 514) | A2-hLambda LC (SEQ ID NO: 429) |
| A2-hIgG4-df-hIL-2 (F42T/I92D) | A2-hIgG4-df-hIL-2 (F42T/I92D) HC (SEQ ID NO: 515) | A2-hLambda LC (SEQ ID NO: 429) |
| A2-hIgG4-df-hIL-2 (F42W/I92D) | A2-hIgG4-df-hIL-2 (F42W/I92D) HC (SEQ ID NO: 516) | A2-hLambda LC (SEQ ID NO: 429) |
| A2-hIgG4-df-hIL-2 (R38E/D84K) | A2-hIgG4-df-hIL-2 (R38E/D84K) HC (SEQ ID NO: 517) | A2-hLambda LC (SEQ ID NO: 429) |
| A2-hIgG4-df-hIL-2 (R38E/I92K) | A2-hIgG4-df-hIL-2 (R38E/I92K) HC (SEQ ID NO: 518) | A2-hLambda LC (SEQ ID NO: 429) |
| C51E6-5-hIgG4-df-hIL-2 (D20A/R38E) | C51E6-5-hIgG4-df-hIL-2 (D20A/R38E) HC (SEQ ID NO: 519) | C51E6-5-hKappa LC (SEQ ID NO: 427) |
| C51E6-5-hIgG4-LE-df-hIL-2 (T3A/D20A/R38E/C125A) | C51E6-5-hIgG4-LE-df-hIL-2 (T3A/D20A/R38E/C125A) HC (SEQ ID NO: 520) | C51E6-5-hKappa LC (SEQ ID NO: 427) |
| C51E6-5-hIgG4-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) | C51E6-5-hIgG4-LAGA-df-hIL-2 (D20A/R38E) HC (SEQ ID NO: 521) | C51E6-5-hKappa LC (SEQ ID NO: 427) |
| 2A3.H7-hIgG4-df-hIL-2 (D20A/R38E) | 2H7-hIgG4-df-hIL-2 (D20A/R38E) HC (SEQ ID NO: 430) | 2A3-hKappa LC (SEQ ID NO: 523) |
| 1H9-hIgG4-df-hIL-2 (D20A/R38E) | 1H9-hIgG4-df-hIL-2 (D20A/R38E) HC (SEQ ID NO: 524) | 1H9-hKappa LC (SEQ ID NO: 525) |
| 1D5-hIgG4-df-hIL-2 (D20A/R38E) | 1D5-hIgG4-df-hIL-2 (D20A/R38E) HC (SEQ ID NO: 526) | 1D5-hKappa LC (SEQ ID NO: 527) |
| 1D5-hIgG4-LE-df-hIL-2 (T3A/D20A/R38E/C125A) | 1D5-hIgG4-LE-df-hIL-2 (T3A/D20A/R38E/C125A) HC (SEQ ID NO: 528) | 1D5-hKappa LC (SEQ ID NO: 527) |
| 1D5-hIgG4-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) | 1D5-hIgG4-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) HC (SEQ ID NO: 529) | 1D5-hKappa LC (SEQ ID NO: 527) |
| 2H7-hIgG1-df-hIL-2 (T3A/D20A/R38E/C125A) | 2H7-hIgG1-df-hIL-2 (T3A/D20A/R38E/C125A) HC (SEQ ID NO: 530) | 2H7-hKappa LC (SEQ ID NO: 425) |
| 2H7-hIgG1-LE-df-hIL-2 (T3A/D20A/R38E/C125A) | 2H7-hIgG1-LE-df-hIL-2 (T3A/D20A/R38E/C125A) HC (SEQ ID NO: 531) | 2H7-hKappa LC (SEQ ID NO: 425) |
| 2H7-hIgG1-LE-df-hIL-2 (T3A/R38E/D84K/C125A) | 2H7-hIgG1-LE-df-hIL-2 (T3A/R38E/D84K/C125A) HC (SEQ ID NO: 533) | 2H7-hKappa LC (SEQ ID NO: 425) |
| 2H7-hIgG4-df-hIL-2 (T3A/R38E/D84K/C125A) | 2H7-hIgG4-df-hIL-2 (T3A/R38E/D84K/C125A) HC (SEQ ID NO: 534) | 2H7-hKappa LC (SEQ ID NO: 425) |
| 2H7-hIgG1-df-hIL-2 (T3A/R38E/I92K/C125A) | 2H7-hIgG1-df-hIL-2 (T3A/R38E/I92K/C125A) HC (SEQ ID NO: 535) | 2H7-hKappa LC (SEQ ID NO: 425) |
| 2H7-hIgG1-LE-df-hIL-2 (T3A/R38E/I92K/C125A) | 2H7-hIgG1-LE-df-hIL-2 (T3A/R38E/I92K/C125A) HC (SEQ ID NO: 536) | 2H7-hKappa LC (SEQ ID NO: 425) |
| 2H7-hIgG4-df-hIL-2 (T3A/R38E/I92K/C125A) | 2H7-hIgG4-df-hIL-2 (T3A/R38E/I92K/C125A) HC (SEQ ID NO: 537) | 2H7-hKappa LC (SEQ ID NO: 425) |
| 2H7-hIgG1-LAGA-df-hIL2 (T3A/D20S/R38E/C125A) | 2H7-hIgG1-LAGA-df-hIL2 (T3A/D20S/R38E/C125A) HC (SEQ ID NO: 538) | 2H7-hKappa LC (SEQ ID NO: 425) |
| 2H7-hIgG1-LAGA-df-hIL2 (T3A/R38E/D84F/C125A) | 2H7-hIgG1-LAGA-df-hIL2 (T3A/R38E/D84F/C125A) HC (SEQ ID NO: 539) | 2H7-hKappa LC (SEQ ID NO: 425) |

TABLE 28-continued

| Exemplary Antibodies | | |
|---|--|--|
| Antibody Name | Heavy chain | Light chain |
| 2H7-hIgG1-LAGA-df-hIL2 (T3A/R38E/192R/C125A) | 2H7-hIgG1-LAGA-df-hIL2 (T3A/R38E/192R/C125A) HC (SEQ ID NO: 540) | 2H7-hKappa LC (SEQ ID NO: 425) |
| 2H7-hIgG1-LAGA-df-hIL2 (T3A/R38E/192E/C125A) | 2H7-hIgG1-LAGA-df-hIL2 (T3A/R38E/192E/C125A) HC (SEQ ID NO: 541) | 2H7-hKappa LC (SEQ ID NO: 425) |
| 2H7-hIgG1-LAGA-df-hIL2 (T3A/R38E/192S/C125A) | 2H7-hIgG1-LAGA-df-hIL2 (T3A/R38E/192S/C125A) HC (SEQ ID NO: 542) | 2H7-hKappa LC (SEQ ID NO: 425) |
| 2H7-hIgG1-LAGA-df-hIL2 (T3A/R38E/192D/C125A) | 2H7-hIgG1-LAGA-df-hIL2 (T3A/R38E/192D/C125A) HC (SEQ ID NO: 543) | 2H7-hKappa LC (SEQ ID NO: 425) |
| 2H7-hIgG1-LAGA-df-hIL2 (T3A/H16E/R38E/C125A) | 2H7-hIgG1-LAGA-df-hIL2 (T3A/H16E/R38E/C125A) HC (SEQ ID NO: 544) | 2H7-hKappa LC (SEQ ID NO: 425) |
| 1H3-hIgG1-L6-hIL-2 (T3A/D20A/R38E/C125A) | 1H3-hIgG1-L6-hIL-2 (T3A/D20A/R38E/C125A) HC (SEQ ID NO: 545) | 1H3-hKappa LC (SEQ ID NO: 374) |
| 1H3-hIgG1-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) | 1H3-hIgG1-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) HC (SEQ ID NO: 546) | 1H3-hKappa LC (SEQ ID NO: 374) |
| C51E6-5-hIgG4/k-LE | C51E6-5-hIgG4/k-LE HC (SEQ ID NO: 547) | C51E6-5-hKappa LC (SEQ ID NO: 427) |
| C51E6-5-hIgG4/k-LAGA | C51E6-5-hIgG4/k-LAGA HC (SEQ ID NO: 548) | C51E6-5-hKappa LC (SEQ ID NO: 427) |
| C51E6-5-hIgG4/k-LEPG | C51E6-5-hIgG4/k-LEPG HC (SEQ ID NO: 549) | C51E6-5-hKappa LC (SEQ ID NO: 427) |
| C51E6-5-hIgG4/k-df-hIL-2 (T3A/D20A/R38E/C125A) | C51E6-5-hIgG4/k-df-hIL-2 (T3A/D20A/R38E/C125A) HC (SEQ ID NO: 550) | C51E6-5-hKappa LC (SEQ ID NO: 427) |
| C51E6-5-hIgG4/k-LEPG-hIL-2 (T3A/D20A/R38E/C125A) | C51E6-5-hIgG4/k-LEPG-hIL-2 (T3A/D20A/R38E/C125A) HC (SEQ ID NO: 551) | C51E6-5-hKappa LC (SEQ ID NO: 427) |
| A2-hIgG4/k-LE | A2-hIgG4/k-LE HC (SEQ ID NO: 552) | A2-hLambda LC (SEQ ID NO: 429) |
| A2-hIgG4/k-LAGA | A2-hIgG4/k-LAGA HC (SEQ ID NO: 553) | A2-hLambda LC (SEQ ID NO: 429) |
| A2-hIgG4/k-LEPG | A2-hIgG4/k-LEPG HC (SEQ ID NO: 554) | A2-hLambda LC (SEQ ID NO: 429) |
| A2-hIgG4/k-df-hIL-2 (T3A/D20A/R38E/C125A) | A2-hIgG4/k-df-hIL-2 (T3A/D20A/R38E/C125A) HC (SEQ ID NO: 555) | A2-hLambda LC (SEQ ID NO: 429) |
| A2-hIgG4/k-LE-df-hIL-2 (T3A/D20A/R38E/C125A) | A2-hIgG4/k-LE-df-hIL-2 (T3A/D20A/R38E/C125A) HC (SEQ ID NO: 556) | A2-hLambda LC (SEQ ID NO: 429) |
| A2-hIgG4/k-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) | A2-hIgG4/k-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) HC (SEQ ID NO: 557) | A2-hLambda LC (SEQ ID NO: 429) |
| A2-hIgG4/k-LEPG-df-hIL-2 (T3A/D20A/R38E/C125A) | A2-hIgG4/k-LEPG-df-hIL-2 (T3A/D20A/R38E/C125A) HC (SEQ ID NO: 558) | A2-hLambda LC (SEQ ID NO: 429) |
| Anti-CD20-hIgG1/k | Anti-CD20-hIgG1/k HC (SEQ ID NO: 560) | Anti-CD20-hKappa LC (SEQ ID NO: 562) |
| Anti-CD20-hIgG1/k-LAGA | Anti-CD20-hIgG1/k-LAGA HC (SEQ ID NO: 561) | Anti-CD20-hKappa LC (SEQ ID NO: 562) |
| 1H3-hIgG1-LAGA-df-hIL-2 (T3A/C125A) | 1H3-hIgG1-LAGA-df-hIL-2 T3A/C125A) HC (SEQ ID NO: 563) | 1H3-hKappa LC (SEQ ID NO: 374) |
| anti-mPD-1 RMP1-14 mIgG2b-N297A | anti-mPD-1 RMP1-14 mIgG2b-N297A HC (SEQ ID NO: 564) | anti-mPD-1 RMP1-14 mKappa LC (SEQ ID NO: 566) |
| anti-mPD-1 RMP1-14 mIgG2b-N297A- L6-hIL-2 (F42K/Y45R/V69R) | anti-mPD-1 RMP1-14 mIgG2b-N297A- L6-hIL-2(F42K/Y45R/V69R) HC (SEQ ID NO: 565) | anti-mPD-1 RMP1-14 mKappa LC (SEQ ID NO: 566) |
| anti-mPD-1 RMP1-30 mIgG2b-N297A | anti-mPD-1 RMP1-30 mIgG2b-N297A HC (SEQ ID NO: 567) | anti-mPD-1 RMP1-30 mKappa LC (SEQ ID NO: 568) |
| anti-mPD-1 RMP1-30 mIgG2b-N297A- L6-hIL-2 (F42K/Y45R/V69R) | anti-mPD-1 RMP1-30 mIgG2b-N297A- L6-hIL-2 (F42K/Y45R/V69R) HC (SEQ ID NO: 569) | anti-mPD-1 RMP1-30 mKappa LC (SEQ ID NO: 568) |
| anti-KLH-C3-mIgG2b-N297A-L6-hIL-2 (F42K/Y45R/V69R) | anti-KLH-C3-mIgG2b-N297A-L6-hIL-2 (F42K/Y45R/V69R) HC (SEQ ID NO: 570) | KLH-C3-mKappa LC (SEQ ID NO: 571) |
| 2D12-hIgG1-L6-hIL-2 | 2D12-hIgG1-L6-hIL-2 HC (SEQ ID NO: 572) | 2D12-hKappa LC (SEQ ID NO: 573) |

TABLE 28-continued

| Exemplary Antibodies | | |
|--|--|--------------------------------------|
| Antibody Name | Heavy chain | Light chain |
| 1H9-hIgG4 | 1H9-hIgG4 HC (SEQ ID NO: 576) | 1H9-hKappa LC (SEQ ID NO: 525) |
| 1D5-hIgG4 | 1D5-hIgG4 HC (SEQ ID NO: 577) | 1D5-hKappa LC (SEQ ID NO: 527) |
| 2A3.H7-hIgG4 | 2H7-hIgG4 HC (SEQ ID NO: 424) | 2A3-hKappa LC (SEQ ID NO: 523) |
| H7-02-hIgG1-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) | H7-02-hIgG1-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) HC (SEQ ID NO: 582) | H7-02-hKappa LC (SEQ ID NO: 583) |
| KLH-C3-hIgG4 | KLH-C3-hIgG4 HC (SEQ ID NO: 585) | KLH-C3-hKappa LC (SEQ ID NO: 586) |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (E15A) | 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (E15A) HC (SEQ ID NO: 587) | 1H3-hkappa LC (SEQ ID NO: 374) |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (D20I) | 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (D20I) HC (SEQ ID NO: 588) | 1H3-hkappa LC (SEQ ID NO: 374) |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (D20S) | 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (D20S) HC (SEQ ID NO: 589) | 1H3-hkappa LC (SEQ ID NO: 374) |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (D20H) | 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (D20H) HC (SEQ ID NO: 590) | 1H3-hkappa LC (SEQ ID NO: 374) |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (D20W) | 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (D20W) HC (SEQ ID NO: 591) | 1H3-hkappa LC (SEQ ID NO: 374) |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (D20Y) | 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (D20Y) HC (SEQ ID NO: 592) | 1H3-hkappa LC (SEQ ID NO: 374) |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (D20R) | 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (D20R) HC (SEQ ID NO: 593) | 1H3-hkappa LC (SEQ ID NO: 374) |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (D20F) | 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (D20F) HC (SEQ ID NO: 594) | 1H3-hkappa LC (SEQ ID NO: 374) |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (D84K) | 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (D84K) HC (SEQ ID NO: 595) | 1H3-hkappa LC (SEQ ID NO: 374) |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (S87A) | 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (S87A) HC (SEQ ID NO: 596) | 1H3-hkappa LC (SEQ ID NO: 374) |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (N88Y) | 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (N88Y) HC (SEQ ID NO: 597) | 1H3-hkappa LC (SEQ ID NO: 374) |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (N88D) | 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (N88D) HC (SEQ ID NO: 598) | 1H3-hkappa LC (SEQ ID NO: 374) |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (N88R) | 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (N88R) HC (SEQ ID NO: 599) | 1H3-hkappa LC (SEQ ID NO: 374) |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (N88E) | 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (N88E) HC (SEQ ID NO: 600) | 1H3-hkappa LC (SEQ ID NO: 374) |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (N88F) | 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (N88F) HC (SEQ ID NO: 601) | 1H3-hkappa LC (SEQ ID NO: 374) |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (N88I) | 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (N88I) HC (SEQ ID NO: 602) | 1H3-hkappa LC (SEQ ID NO: 374) |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (I92A) | 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (I92A) HC (SEQ ID NO: 603) | 1H3-hkappa LC (SEQ ID NO: 374) |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (E95A) | 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (E95A) HC (SEQ ID NO: 604) | 1H3-hkappa LC (SEQ ID NO: 374) |
| 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (E95K) | 1H3-hIgG1-L6-hCD25(1-164)-L20-hIL-2 (E95K) HC (SEQ ID NO: 605) | 1H3-hkappa LC (SEQ ID NO: 374) |
| H7-02-hIgG4 | H7-02-hIgG4 HC (SEQ ID NO: 373) | H7-02 hKappa LC (SEQ ID NO: 607) |
| H7-632-hIgG1-LAGA-df-hIL-2 (T3A/C125A) | H7-632-hIgG1-LAGA-df-hIL-2 (T3A/C125A) HC (SEQ ID NO: 431) | H7-632 LC (SEQ ID NO: 415) |
| 1H3-hIgG1-LAGA-L6-hIL-2 (T3A/D20A/R38E/C125A) | 1H3-hIgG1-LAGA-L6-hIL-2 (T3A/D20A/R38E/C125A) (SEQ ID NO: 522) | 1H3-hKappa LC (SEQ ID NO: 374) |
| 1H3-hIgG1 | 1H3-hIgG1 HC (SEQ ID NO: 379) | 1H3-hKappa LC (SEQ ID NO: 374) |
| H7-767 | H7-767 HC (SEQ ID NO: 532) | H7-632 LC (SEQ ID NO: 415) |
| Anti-hPD-1 #1 | Anti-hPD-1 #1 HC (SEQ ID NO: 559) | Anti-hPD-1#1-hKappa (SEQ ID NO: 452) |
| Anti-hPD-1 #2 | Anti-hPD-1 #2 HC (SEQ ID NO: 578) | Anti-hPD-1 #2 LC (SEQ ID NO: 579) |
| 2H7-hIgG4-LE-df-hIL-2 (T3A/R38E/I92K/C125A) | 2H7-hIgG4-LE-df-hIL-2 (T3A/R38E/I92K/C125A) HC (SEQ ID NO: 475) | 2H7-hKappa LC (SEQ ID NO: 425) |

TABLE 29

| Sequences | | |
|------------|------------|---|
| SEQ ID NO: | Name | Sequence |
| 1 | hIL-2 F42K | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTKKFYMPKKATELKHLCLEEBELKPLEEV LNLAQSKNFHLRPRDLISININVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 2 | hIL-2 V69A | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTFKPFYMPKKATELKHLCLEEBELKPLEEA LNLAQSKNFHLRPRDLISININVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |

TABLE 29-continued

| Sequences | | |
|------------|--------------------|--|
| SEQ ID NO: | Name | Sequence |
| 103 | hIL-2 N88D | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISDINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 104 | hIL-2 N88R | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISRINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 105 | hIL-2 N88E | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISEINVIVLELKGSETTEMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 106 | hIL-2 N88F | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISFINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 107 | hIL-2 N88I | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISIIINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 108 | hIL-2 I92A | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVAVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 109 | hIL-2 I92Y | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 110 | hIL-2 I92S | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVSLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 111 | hIL-2 I92F | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVFVLELKGSETTEMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 112 | hIL-2 I92R | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINRVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 113 | hIL-2 I92D | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTEMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 114 | hIL-2 I92E | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVEVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 115 | hIL-2 E95A | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINIVLALKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 116 | hIL-2 E95R | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINIVLRLKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 117 | hIL-2 E95K | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINIVLKLKGSETTEMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 118 | hIL-2 D20Y/H16E | APTSSSTKKTQLQLEHLLLYLQMI LNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINIVLELKGSETTEMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 119 | hIL-2 D20Y/H16A | APTSSSTKKTQLQLEALLLYLQMI LNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINIVLELKGSETTEMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 120 | hIL-2 D20Y/H16Y | APTSSSTKKTQLQLEYLLLYLQMI LNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINIVLELKGSETTEMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 121 | hIL-2 D20Y/I92A | APTSSSTKKTQLQLEHLLLYLQMI LNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVAVLELKGSETTEMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 122 | hIL-2 D20Y/I92S | APTSSSTKKTQLQLEHLLLYLQMI LNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVSLELKGSETTEMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 123 | hIL-2 D20Y/I92R | APTSSSTKKTQLQLEHLLLYLQMI LNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINRVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 124 | hIL-2 D20Y/E95R | APTSSSTKKTQLQLEHLLLYLQMI LNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINIVLRLKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 125 | hIL-2 D20Y/E95A | APTSSSTKKTQLQLEHLLLYLQMI LNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINIVLALKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 126 | hCD25 (1-164) | ELCDDDPPEIPHATFKAMAYKEGTMLNCECKRGERRIKSGSLYMLCTGNSHSHSWDNQCQCTSSATRNT TKQVTPQPEEQKERKTEMQSPMQPVDQASLPGHCREPPPWENEATERIYHFPVVGQMVYQCVQGYRAL HRGPAESVCKMTHGKTRWTPQLICT |

TABLE 29-continued

| Sequences | | |
|------------|--------------------|---|
| SEQ ID NO: | Name | Sequence |
| 127 | hIL-2 F42D/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTEMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 128 | hIL-2 F42R/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTRKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTEMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 129 | hIL-2 F42K/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTKKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 130 | hIL-2 F42A/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTAKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 131 | hIL-2 F42H/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTHKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 132 | hIL-2 Y45R/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFKFRMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTEMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 133 | hIL-2 Y45K/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFKFKMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTEMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 134 | hIL-2 R38N/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTNMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 135 | hIL-2 R38G/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTGMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTEMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 136 | hIL-2 R38H/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTHMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTEMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 137 | hIL-2 R38I/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTMMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 138 | hIL-2 R38L/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTLMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTEMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 139 | hIL-2 R38M/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTMMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 140 | hIL-2 R38F/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTFMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTEMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 141 | hIL-2 R38P/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTPMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTEMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 142 | hIL-2 R38S/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTSMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 143 | hIL-2 R38T/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTMMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTEMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 144 | hIL-2 R38W/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTMMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTEMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 145 | hIL-2 R38Y/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTYMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 146 | hIL-2 R38V/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTVMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTEMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 147 | hIL-2 R38A/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTAMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTEMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 148 | hIL-2 R38Q/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTQMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTEMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 149 | hIL-2 D20A/R38E | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTEMMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 150 | hIL-2 R38D/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTDMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTEMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 151 | hIL-2 K43E/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFEFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |

TABLE 29-continued

| Sequences | | |
|------------|--------------------|---|
| SEQ ID NO: | Name | Sequence |
| 152 | hIL-2 E61A/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFKPYMPKKATELKHLCLEAEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 153 | hIL-2 E62A/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFKPYMPKKATELKHLCLEAEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 154 | hIL-2 E62Y/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFKPYMPKKATELKHLCLEEYLKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 155 | hIL-2 L72D/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFKPYMPKKATELKHLCLEEEELKPLEEV LNDAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 156 | hIL-2 L72H/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFKPYMPKKATELKHLCLEEEELKPLEEV LNHAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 157 | hIL-2 L72R/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFKPYMPKKATELKHLCLEEEELKPLEEV LNRAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 158 | hIL-2 F42D/I92D | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKLTRMLTKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 159 | hIL-2 F42R/I92D | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKLTRMLTRKPYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 160 | hIL-2 F42H/I92D | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKLTRMLTHKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 161 | hIL-2 F42A/I92D | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKLTRMLTAKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 162 | hIL-2 K43E/I92D | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKLTRMLTFEFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 163 | hIL-2 Y45R/I92D | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKLTRMLTFKFRMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 164 | hIL-2 Y45K/I92D | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKLTRMLTFKFKMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 165 | hIL-2 E62A/I92D | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKLTRMLTFKPYMPKKATELKHLCLEAEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 166 | hIL-2 E62Y/I92D | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKLTRMLTFKPYMPKKATELKHLCLEEYLKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 167 | hIL-2 L72D/I92D | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKLTRMLTFKPYMPKKATELKHLCLEEEELKPLEEV LNDAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 168 | hIL-2 L72H/I92D | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKLTRMLTFKPYMPKKATELKHLCLEEEELKPLEEV LNHAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 169 | hIL-2 L72R/I92D | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKLTRMLTFKPYMPKKATELKHLCLEEEELKPLEEV LNRAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 170 | hIL-2 R38D/I92D | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKLTDMLTFKPYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 171 | hIL-2 R38E/I92D | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKLTEMMLTFKPYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 172 | hIL-2 R38Q/I92D | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKLQMLTFKPYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 173 | hIL-2 R38A/I92D | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKLAMLTFKPYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 174 | hIL-2 R38E/N88R | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKLTEMMLTFKPYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 175 | hIL-2 R38E/D84R | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKLTEMMLTFKPYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 176 | hIL-2 R38E/D84K | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKLTEMMLTFKPYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |

TABLE 29-continued

| Sequences | | |
|---------------|-----------------------------|---|
| SEQ ID NO: | Name | Sequence |
| 177 | hIL-2 F42A/Y45R/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTAKFRMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 178 | hIL-2 F42H/Y45R/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTHKFRMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 179 | hIL-2 R38D/E61R/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTDMLTFKFYMPKKATELKHLCLEERELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 180 | hIL-2 R38E/E61R/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTEMMLTFKFYMPKKATELKHLCLEERELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 181 | hIL-2 R38Q/E61R/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLQMLTFKFYMPKKATELKHLCLEERELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 182 | hIL-2 R38A/E61R/D20A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLAMLTFKFYMPKKATELKHLCLEERELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 183 | hIL-2 R38A/D20A/E95A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLAMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLALKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 184 | hIL-2 D20A/E95A/R38D | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTDMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLALKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 185 | hIL-2 D20A/ E95A/R38E | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTEMMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLALKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 186 | hIL-2 D20A/E95A/R38Q | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLQMLTFKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLALKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 187 | hIL-2 D20A/E95A/F42R | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTRKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLALKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 188 | hIL-2 D20A/E95A/F42A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTAKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLALKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 189 | hIL-2 D20A/E95A/ F42D | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTDKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLALKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 190 | hIL-2 D20A/E95A/ F42H | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTHKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLALKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 191 | hIL-2 D20A/E95A/F42K | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLALKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 192 | hIL-2 D20A/E95A/ K43A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFAFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLALKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 193 | hIL-2 D20A/E95A/ K43E | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFEFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLALKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 194 | hIL-2 D20A/E95A/ K43Q | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFQFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLALKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 195 | hIL-2 D20A/E95A/ Y45A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFKFAFMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLALKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 196 | hIL-2 D20A/E95A/ Y45K | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFKFKMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLALKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 197 | hIL-2 D20A/E95A/ 45S | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFKESMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLALKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 198 | hIL-2 D20A/E95A/ Y45R | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFKFRMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLALKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |

TABLE 29-continued

| Sequences | | |
|------------|---|--|
| SEQ ID NO: | Name | Sequence |
| 199 | hIL-2 D20A/E95A/ E61A | APTSSSTKKTQLQLEHLLALQMI L N G I N N Y K N P K L T R M L T P K F Y M P K K A T E L K H L Q C L E A E L K P L E E V L N L A Q S K N F H L R P R D L I S N I N V I V L A L K G S E T T F M C E Y A D E T A T I V E F L N R W I T F C Q S I I S T L T |
| 200 | hIL-2 D20A/E95A/ E62A | APTSSSTKKTQLQLEHLLALQMI L N G I N N Y K N P K L T R M L T P K F Y M P K K A T E L K H L Q C L E E A L K P L E E V L N L A Q S K N F H L R P R D L I S N I N V I V L A L K G S E T T E M C E Y A D E T A T I V E F L N R W I T F C Q S I I S T L T |
| 201 | hIL-2 D20A/E95A/E62R | APTSSSTKKTQLQLEHLLALQMI L N G I N N Y K N P K L T R M L T P K F Y M P K K A T E L K H L Q C L E E R L K P L E E V L N L A Q S K N F H L R P R D L I S N I N V I V L A L K G S E T T F M C E Y A D E T A T I V E F L N R W I T F C Q S I I S T L T |
| 202 | hIL-2 D20A/E95A/ E62K | APTSSSTKKTQLQLEHLLALQMI L N G I N N Y K N P K L T R M L T P K F Y M P K K A T E L K H L Q C L E E E K L K P L E E V L N L A Q S K N F H L R P R D L I S N I N V I V L A L K G S E T T E M C E Y A D E T A T I V E F L N R W I T F C Q S I I S T L T |
| 203 | hIL-2 D20A/E95A/ E62Y | APTSSSTKKTQLQLEHLLALQMI L N G I N N Y K N P K L T R M L T P K F Y M P K K A T E L K H L Q C L E E Y L K P L E E V L N L A Q S K N F H L R P R D L I S N I N V I V L A L K G S E T T F M C E Y A D E T A T I V E F L N R W I T F C Q S I I S T L T |
| 204 | hIL-2 D20A/E95A/ E68Y | APTSSSTKKTQLQLEHLLALQMI L N G I N N Y K N P K L T R M L T P K F Y M P K K A T E L K H L Q C L E E E L K P L E Y V L N L A Q S K N F H L R P R D L I S N I N V I V L A L K G S E T T F M C E Y A D E T A T I V E F L N R W I T F C Q S I I S T L T |
| 205 | hIL-2 D20A/E95A/E68A | APTSSSTKKTQLQLEHLLALQMI L N G I N N Y K N P K L T R M L T P K F Y M P K K A T E L K H L Q C L E E E L K P L E A V L N L A Q S K N F H L R P R D L I S N I N V I V L A L K G S E T T F M C E Y A D E T A T I V E F L N R W I T F C Q S I I S T L T |
| 206 | hIL-2 D20A/E95A/ E68L | APTSSSTKKTQLQLEHLLALQMI L N G I N N Y K N P K L T R M L T P K F Y M P K K A T E L K H L Q C L E E E L K P L E L V L N L A Q S K N F H L R P R D L I S N I N V I V L A L K G S E T T E M C E Y A D E T A T I V E F L N R W I T F C Q S I I S T L T |
| 207 | hIL-2 D20A/E95A/ L72Y | APTSSSTKKTQLQLEHLLALQMI L N G I N N Y K N P K L T R M L T P K F Y M P K K A T E L K H L Q C L E E E L K P L E E V L N Y A Q S K N F H L R P R D L I S N I N V I V L A L K G S E T T F M C E Y A D E T A T I V E F L N R W I T F C Q S I I S T L T |
| 208 | hIL-2 D20A/E95A/ L72R | APTSSSTKKTQLQLEHLLALQMI L N G I N N Y K N P K L T R M L T P K F Y M P K K A T E L K H L Q C L E E E L K P L E E V L N R A Q S K N F H L R P R D L I S N I N V I V L A L K G S E T T E M C E Y A D E T A T I V E F L N R W I T F C Q S I I S T L T |
| 209 | hIL-2 D20A/E95A/ L72A | APTSSSTKKTQLQLEHLLALQMI L N G I N N Y K N P K L T R M L T P K F Y M P K K A T E L K H L Q C L E E E L K P L E E V L N A A Q S K N F H L R P R D L I S N I N V I V L A L K G S E T T F M C E Y A D E T A T I V E F L N R W I T F C Q S I I S T L T |
| 210 | hIL-2 D20A/E95A/L72D | APTSSSTKKTQLQLEHLLALQMI L N G I N N Y K N P K L T R M L T P K F Y M P K K A T E L K H L Q C L E E E L K P L E E V L N D A Q S K N F H L R P R D L I S N I N V I V L A L K G S E T T F M C E Y A D E T A T I V E F L N R W I T F C Q S I I S T L T |
| 211 | hIL-2 D20A/E95A/ L72H | APTSSSTKKTQLQLEHLLALQMI L N G I N N Y K N P K L T R M L T P K F Y M P K K A T E L K H L Q C L E E E L K P L E E V L N H A Q S K N F H L R P R D L I S N I N V I V L A L K G S E T T F M C E Y A D E T A T I V E F L N R W I T F C Q S I I S T L T |
| 212 | hIL-2 D20A/E95A/ L72F | APTSSSTKKTQLQLEHLLALQMI L N G I N N Y K N P K L T R M L T P K F Y M P K K A T E L K H L Q C L E E E L K P L E E V L N F A Q S K N F H L R P R D L I S N I N V I V L A L K G S E T T F M C E Y A D E T A T I V E F L N R W I T F C Q S I I S T L T |
| 213 | hIL-2 F42K/Y45R/D20A/ S87A | APTSSSTKKTQLQLEHLLALQMI L N G I N N Y K N P K L T R M L T K K F R M P K K A T E L K H L Q C L E E E L K P L E E V L N L A Q S K N F H L R P R D L I A N I N V I V L E L K G S E T T E M C E Y A D E T A T I V E F L N R W I T F C Q S I I S T L T |
| 214 | hIL-2 F42K/Y45R/D20A/ E95A | APTSSSTKKTQLQLEHLLALQMI L N G I N N Y K N P K L T R M L T K K E R M P K K A T E L K H L Q C L E E E L K P L E E V L N L A Q S K N F H L R P R D L I S N I N V I V L A L K G S E T T E M C E Y A D E T A T I V E F L N R W I T F C Q S I I S T L T |
| 215 | hIL-2 D20A/R38E/C125 A | APTSSSTKKTQLQLEHLLALQMI L N G I N N Y K N P K L T E M L T P K F Y M P K K A T E L K H L Q C L E E E L K P L E E V L N L A Q S K N F H L R P R D L I S N I N V I V L E L K G S E T T F M C E Y A D E T A T I V E F L N R W I T F A Q S I I S T L T |
| 216 | hIL-2 T3A/D20A/R38E | A P A S S T K K T Q L Q L E H L L A L Q M I L N G I N N Y K N P K L T E M L T P K F Y M P K K A T E L K H L Q C L E E E L K P L E E V L N L A Q S K N F H L R P R D L I S N I N V I V L E L K G S E T T F M C E Y A D E T A T I V E F L N R W I T F C Q S I I S T L T |
| 217 | hIL-2 T3A/D20A/R38E/ C125A (IL-2-AAEA) | A P A S S T K K T Q L Q L E H L L A L Q M I L N G I N N Y K N P K L T E M L T P K F Y M P K K A T E L K H L Q C L E E E L K P L E E V L N L A Q S K N F H L R P R D L I S N I N V I V L E L K G S E T T E M C E Y A D E T A T I V E F L N R W I T F A Q S I I S T L T |

TABLE 29-continued

| Sequences | | |
|------------|-------------------------------|---|
| SEQ ID NO: | Name | Sequence |
| 218 | hIL-2 Δ1-3APT/D20A/R38E | SSSTKKTQLQLEHLLALQMI LNGINNYKNPKL E MLTFKFYMPKKATELKHLCLEEEELKPLEEVLNLAQSKNFHLRPRDLISNINIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSIISTLT |
| 219 | hIL-2 Δ1-3APT/D20A/R38E/C125A | SSSTKKTQLQLEHLLALQMI LNGINNYKNPKL E MLTFKFYMPKKATELKHLCLEEEELKPLEEVLNLAQSKNFHLRPRDLISNINIVLELKGSETTEMCEYADETATIVEFLNRWITFAQSIISTLT |
| 220 | hIL-2 R38E/Q22A | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKL E MLTFKFYMPKKATELKHLCLEEEELKPLEEVLNLAQSKNFHLRPRDLISNINIVLELKGSETTEMCEYADETATIVEFLNRWITFCQSIISTLT |
| 221 | hIL-2 R38E/T123A | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKL E MLTFKFYMPKKATELKHLCLEEEELKPLEEVLNLAQSKNFHLRPRDLISNINIVLELKGSETTFMCEYADETATIVEFLNRWITAFQSIISTLT |
| 222 | hIL-2 R38E/I129A | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKL E MLTFKFYMPKKATELKHLCLEEEELKPLEEVLNLAQSKNFHLRPRDLISNINIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI A STLT |
| 223 | hIL-2 R38E/S130A | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKL E MLTFKFYMPKKATELKHLCLEEEELKPLEEVLNLAQSKNFHLRPRDLISNINIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI I ATLT |
| 224 | hIL-2 R38E/Q126A | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKL E MLTFKFYMPKKATELKHLCLEEEELKPLEEVLNLAQSKNFHLRPRDLISNINIVLELKGSETTFMCEYADETATIVEFLNRWITFC A SIISTLT |
| 225 | hIL-2 R38E/Q126D | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKL E MLTFKFYMPKKATELKHLCLEEEELKPLEEVLNLAQSKNFHLRPRDLISNINIVLELKGSETTEMCEYADETATIVEFLNRWITFC D SIISTLT |
| 226 | hIL-2 R38E/Q126V | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKL E MLTFKFYMPKKATELKHLCLEEEELKPLEEVLNLAQSKNFHLRPRDLISNINIVLELKGSETTEMCEYADETATIVEFLNRWITFC V SIISTLT |
| 227 | hIL-2 R38E/Q22A/S130A | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKL E MLTFKFYMPKKATELKHLCLEEEELKPLEEVLNLAQSKNFHLRPRDLISNINIVLELKGSETTEMCEYADETATIVEFLNRWITFCQSI I ATLT |
| 228 | hIL-2 F42K/Y45R/Q126D | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKL TRMLTKKFRMP KKATELKHLCLEEEELKPLEEVLNLAQSKNFHLRPRDLISNINIVLELKGSETTFMCEYADETATIVEFLNRWITFC D SIISTLT |
| 229 | hIL-2 D20A/E95A/Q126D | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKL TRMLTFKFYMP KKATELKHLCLEEEELKPLEEVLNLAQSKNFHLRPRDLISNINIVL A LKGSETTFMCEYADETATIVEFLNRWITFC D SIISTLT |
| 230 | hIL-2 D20A/E61R | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKL TRMLTFKFYMP KKATELKHLCLE R ELKPLEEVLNLAQSKNFHLRPRDLISNINIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSIISTLT |
| 231 | hIL-2 D20A/E61N | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKL TRMLTFKFYMP KKATELKHLCLE N ELKPLEEVLNLAQSKNFHLRPRDLISNINIVLELKGSETTEMCEYADETATIVEFLNRWITFCQSIISTLT |
| 232 | hIL-2 D20A/E61D | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKL TRMLTFKFYMP KKATELKHLCLE D ELKPLEEVLNLAQSKNFHLRPRDLISNINIVLELKGSETTEMCEYADETATIVEFLNRWITFCQSIISTLT |
| 233 | hIL-2 D20A/E61Q | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKL TRMLTFKFYMP KKATELKHLCLE Q ELKPLEEVLNLAQSKNFHLRPRDLISNINIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSIISTLT |
| 234 | hIL-2 D20A/E61G | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKL TRMLTFKFYMP KKATELKHLCLE G ELKPLEEVLNLAQSKNFHLRPRDLISNINIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSIISTLT |
| 235 | hIL-2 D20A/E61H | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKL TRMLTFKFYMP KKATELKHLCLE H ELKPLEEVLNLAQSKNFHLRPRDLISNINIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSIISTLT |
| 236 | hIL-2 D20A/E61I | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKL TRMLTFKFYMP KKATELKHLCLE I ELKPLEEVLNLAQSKNFHLRPRDLISNINIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSIISTLT |
| 237 | hIL-2 D20A/E61L | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKL TRMLTFKFYMP KKATELKHLCLE L ELKPLEEVLNLAQSKNFHLRPRDLISNINIVLELKGSETTEMCEYADETATIVEFLNRWITFCQSIISTLT |
| 238 | hIL-2 D20A/E61K | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKL TRMLTFKFYMP KKATELKHLCLE K ELKPLEEVLNLAQSKNFHLRPRDLISNINIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSIISTLT |
| 239 | hIL-2 D20A/E61M | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKL TRMLTFKFYMP KKATELKHLCLE M ELKPLEEVLNLAQSKNFHLRPRDLISNINIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSIISTLT |
| 240 | hIL-2 D20A/E61F | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKL TRMLTFKFYMP KKATELKHLCLE F ELKPLEEVLNLAQSKNFHLRPRDLISNINIVLELKGSETTEMCEYADETATIVEFLNRWITFCQSIISTLT |

TABLE 29-continued

| Sequences | | |
|---------------|--------------------|---|
| SEQ ID NO: | Name | Sequence |
| 241 | hIL-2 D20A/E61P | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLEPELKPLEE LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 242 | hIL-2 D20A/E61S | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLESELKPLEE LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 243 | hIL-2 D20A/E61T | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLETELKPLEE LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 244 | hIL-2 D20A/E61W | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLEWELKPLEE LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 245 | hIL-2 D20A/E61Y | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLEYLELKPLEE LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 246 | hIL-2 D20A/E61V | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFKFYMPKKATELKHLCLEVELKPLEE LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 247 | hIL-2 D20A/F42N | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTNKFYMPKKATELKHLCLEELKPLEE LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 248 | hIL-2 D20A/F42Q | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTQKFYMPKKATELKHLCLEELKPLEE LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 249 | hIL-2 D20A/F42E | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTEKFYMPKKATELKHLCLEELKPLEE LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 250 | hIL-2 D20A/F42G | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTGKFYMPKKATELKHLCLEELKPLEE LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 251 | hIL-2 D20A/F42I | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTIKFYMPKKATELKHLCLEELKPLEE LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 252 | hIL-2 D20A/F42L | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTLKFYMPKKATELKHLCLEELKPLEE LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 253 | hIL-2 D20A/F42M | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTMKFYMPKKATELKHLCLEELKPLEE LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 254 | hIL-2 D20A/F42P | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTPKFYMPKKATELKHLCLEELKPLEE LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 255 | hIL-2 D20A/F42S | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTSKFYMPKKATELKHLCLEELKPLEE LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 256 | hIL-2 D20A/F42T | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTTKFYMPKKATELKHLCLEELKPLEE LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 257 | hIL-2 D20A/F42W | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTWKFYMPKKATELKHLCLEELKPLEE LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 258 | hIL-2 D20A/F42Y | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTYKFYMPKKATELKHLCLEELKPLEE LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 259 | hIL-2 D20A/F42V | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTVKFYMPKKATELKHLCLEELKPLEE LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 260 | hIL-2 D20A/Y45A | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFKFPMPKKATELKHLCLEELKPLEE LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 261 | hIL-2 D20A/Y45N | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFKFNMPKKATELKHLCLEELKPLEE LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 262 | hIL-2 D20A/Y45D | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFKFDMPKKATELKHLCLEELKPLEE LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 263 | hIL-2 D20A/Y45Q | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFKFMPPKKATELKHLCLEELKPLEE LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 264 | hIL-2 D20A/Y45E | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFKFEPPKKATELKHLCLEELKPLEE LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 265 | hIL-2 D20A/Y45G | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFKFGMPKKATELKHLCLEELKPLEE LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |

TABLE 29-continued

| Sequences | | |
|------------|--------------------|--|
| SEQ ID NO: | Name | Sequence |
| 266 | hIL-2 D20A/Y45H | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFKFMPPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 267 | hIL-2 D20A/Y45I | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFKFMPPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 268 | hIL-2 D20A/Y45L | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFKFLMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 269 | hIL-2 D20A/Y45M | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFKFMPPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 270 | hIL-2 D20A/Y45F | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFKFMPPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 271 | hIL-2 D20A/Y45P | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFKFMPPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 272 | hIL-2 D20A/Y45S | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFKFSMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 273 | hIL-2 D20A/Y45T | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFKFTMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 274 | hIL-2 D20A/Y45W | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFKFWMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 275 | hIL-2 D20A/Y45V | APTSSSTKKTQLQLEHLLALQMI LNGINNYKNPKLTRMLTFKFMPPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 276 | hIL-2 I92D/F42N | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKLTRMLTNKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 277 | hIL-2 I92D/F42Q | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKLTRMLTQKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 278 | hIL-2 I92D/F42E | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKLTRMLTEKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 279 | hIL-2 I92D/F42G | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKLTRMLTGKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 280 | hIL-2 I92D/F42I | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKLTRMLTIKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 281 | hIL-2 I92D/F42L | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKLTRMLTLKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 282 | hIL-2 I92D/F42K | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKLTRMLTKKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 283 | hIL-2 I92D/F42M | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKLTRMLTMKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 284 | hIL-2 I92D/F42P | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKLTRMLTPKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 285 | hIL-2 I92D/F42S | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKLTRMLTSKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 286 | hIL-2 I92D/F42T | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKLTRMLTTKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 287 | hIL-2 I92D/F42W | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKLTRMLTWKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 288 | hIL-2 I92D/F42Y | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKLTRMLTYKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 289 | hIL-2 I92D/F42V | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKLTRMLTVKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 290 | hIL-2 I92D/Y45A | APTSSSTKKTQLQLEHLLDLQMI LNGINNYKNPKLTRMLTFKAMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |

TABLE 29-continued

| Sequences | | |
|------------|--------------------|--|
| SEQ ID NO: | Name | Sequence |
| 291 | hIL-2 I92D/Y45N | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTFKENMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 292 | hIL-2 I92D/Y45D | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTFKEDMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 293 | hIL-2 I92D/Y45Q | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTFKQMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 294 | hIL-2 I92D/Y45E | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTFKFMPPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 295 | hIL-2 I92D/Y45G | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTFKFGMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 296 | hIL-2 I92D/Y45H | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTFKFMPPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 297 | hIL-2 I92D/Y45I | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTFKFI MPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 298 | hIL-2 I92D/Y45L | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTEKELMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 299 | hIL-2 I92D/Y45M | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTFKEMMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 300 | hIL-2 I92D/Y45F | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTFKFMPPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 301 | hIL-2 I92D/Y45P | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTFKFMPPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 302 | hIL-2 I92D/Y45S | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTEKFSMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 303 | hIL-2 I92D/Y45T | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTFKFTMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 304 | hIL-2 I92D/Y45W | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTFKFWMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 305 | hIL-2 I92D/Y45V | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTFKFMPPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINVDVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 306 | hIL-2 R38E/D20H | APTSSSTKKTQLQLEHLLHLQMI LNGINNYKNPKLTEMMLTFKFMPPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 307 | hIL-2 R38E/D20S | APTSSSTKKTQLQLEHLLLSLQMI LNGINNYKNPKLTEMMLTFKFMPPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 308 | hIL-2 F42A/N88R | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTAKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 309 | hIL-2 F42A/N88D | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTAKFYMPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 310 | hIL-2 R38E/D84A | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTEMMLTFKFMPPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 311 | hIL-2 R38E/D84N | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTEMMLTFKFMPPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 312 | hIL-2 R38E/D84Q | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTEMMLTFKFMPPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 313 | hIL-2 R38E/D84E | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTEMMLTFKFMPPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 314 | hIL-2 R38E/D84G | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTEMMLTFKFMPPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |
| 315 | hIL-2 R38E/D84H | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTEMMLTFKFMPPKKATELKHLCLEEEELKPLEEV LNLAQSKNFHLRPRDLISNINIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSI ISTLT |

TABLE 29-continued

| Sequences | | |
|---------------|--------------------|---|
| SEQ ID NO: | Name | Sequence |
| 316 | hIL-2 R38E/D84I | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTEM LTFKFYMPKKATELKH LQCLEEEELKPLEEV LNLAQSKNFHLRPRILISNINIVLELKGSETTFMCEYADETAT IVEFLNRWITFCQSI ISTLT |
| 317 | hIL-2 R38E/D84L | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTEM LTFKFYMPKKATELKH LQCLEEEELKPLEEV LNLAQSKNFHLRPRLLISNINIVLELKGSETTFMCEYADETAT IVEFLNRWITFCQSI ISTLT |
| 318 | hIL-2 R38E/D84M | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTEM LTFKFYMPKKATELKH LQCLEEEELKPLEEV LNLAQSKNFHLRPRMLISNINIVLELKGSETTFMCEYADETAT IVEFLNRWITFCQSI ISTLT |
| 319 | hIL-2 R38E/D84F | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTEM LTFKFYMPKKATELKH LQCLEEEELKPLEEV LNLAQSKNFHLRPRFLISNINIVLELKGSETTFMCEYADETAT IVEFLNRWITFCQSI ISTLT |
| 320 | hIL-2 R38E/D84P | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTEM LTFKFYMPKKATELKH LQCLEEEELKPLEEV LNLAQSKNFHLRPRPLISNINIVLELKGSETTFMCEYADETAT IVEFLNRWITFCQSI ISTLT |
| 321 | hIL-2 R38E/D84S | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTEM LTFKFYMPKKATELKH LQCLEEEELKPLEEV LNLAQSKNFHLRPRSLISNINIVLELKGSETTFMCEYADETAT IVEFLNRWITFCQSI ISTLT |
| 322 | hIL-2 R38E/D84T | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTEM LTFKFYMPKKATELKH LQCLEEEELKPLEEV LNLAQSKNFHLRPRTLISNINIVLELKGSETTFMCEYADETAT IVEFLNRWITFCQSI ISTLT |
| 323 | hIL-2 R38E/D84W | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTEM LTFKFYMPKKATELKH LQCLEEEELKPLEEV LNLAQSKNFHLRPRWLLISNINIVLELKGSETTFMCEYADETAT IVEFLNRWITFCQSI ISTLT |
| 324 | hIL-2 R38E/D84Y | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTEM LTFKFYMPKKATELKH LQCLEEEELKPLEEV LNLAQSKNFHLRPRYLLISNINIVLELKGSETTFMCEYADETAT IVEFLNRWITFCQSI ISTLT |
| 325 | hIL-2 R38E/D84V | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTEM LTFKFYMPKKATELKH LQCLEEEELKPLEEV LNLAQSKNFHLRPRVLLISNINIVLELKGSETTFMCEYADETAT IVEFLNRWITFCQSI ISTLT |
| 326 | hIL-2 R38E/I92A | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTEM LTFKFYMPKKATELKH LQCLEEEELKPLEEV LNLAQSKNFHLRPRDLLISNINIVAVLELKGSETTFMCEYADETAT IVEFLNRWITFCQSI ISTLT |
| 327 | hIL-2 R38E/I92R | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTEM LTFKFYMPKKATELKH LQCLEEEELKPLEEV LNLAQSKNFHLRPRDLLISNINIVRVLELKGSETTFMCEYADETAT IVEFLNRWITFCQSI ISTLT |
| 328 | hIL-2 R38E/I92N | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTEM LTFKFYMPKKATELKH LQCLEEEELKPLEEV LNLAQSKNFHLRPRDLLISNINIVVLELKGSETTFMCEYADETAT IVEFLNRWITFCQSI ISTLT |
| 329 | hIL-2 R38E/I92Q | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTEM LTFKFYMPKKATELKH LQCLEEEELKPLEEV LNLAQSKNFHLRPRDLLISNINIVQVLELKGSETTFMCEYADETAT IVEFLNRWITFCQSI ISTLT |
| 330 | hIL-2 R38E/I92E | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTEM LTFKFYMPKKATELKH LQCLEEEELKPLEEV LNLAQSKNFHLRPRDLLISNINIVVLELKGSETTFMCEYADETAT IVEFLNRWITFCQSI ISTLT |
| 331 | hIL-2 R38E/I92G | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTEM LTFKFYMPKKATELKH LQCLEEEELKPLEEV LNLAQSKNFHLRPRDLLISNINIVGVLELKGSETTFMCEYADETAT IVEFLNRWITFCQSI ISTLT |
| 332 | hIL-2 R38E/I92H | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTEM LTFKFYMPKKATELKH LQCLEEEELKPLEEV LNLAQSKNFHLRPRDLLISNINIVHVLELKGSETTFMCEYADETAT IVEFLNRWITFCQSI ISTLT |
| 333 | hIL-2 R38E/I92L | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTEM LTFKFYMPKKATELKH LQCLEEEELKPLEEV LNLAQSKNFHLRPRDLLISNINIVLVLELKGSETTFMCEYADETAT IVEFLNRWITFCQSI ISTLT |
| 334 | hIL-2 R38E/I92K | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTEM LTFKFYMPKKATELKH LQCLEEEELKPLEEV LNLAQSKNFHLRPRDLLISNINIVKLELKGSETTFMCEYADETAT IVEFLNRWITFCQSI ISTLT |
| 335 | hIL-2 R38E/I92M | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTEM LTFKFYMPKKATELKH LQCLEEEELKPLEEV LNLAQSKNFHLRPRDLLISNINIVVLELKGSETTFMCEYADETAT IVEFLNRWITFCQSI ISTLT |
| 336 | hIL-2 R38E/I92F | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTEM LTFKFYMPKKATELKH LQCLEEEELKPLEEV LNLAQSKNFHLRPRDLLISNINIVVLELKGSETTFMCEYADETAT IVEFLNRWITFCQSI ISTLT |
| 337 | hIL-2 R38E/I92P | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTEM LTFKFYMPKKATELKH LQCLEEEELKPLEEV LNLAQSKNFHLRPRDLLISNINIVVLELKGSETTFMCEYADETAT IVEFLNRWITFCQSI ISTLT |
| 338 | hIL-2 R38E/I92S | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTEM LTFKFYMPKKATELKH LQCLEEEELKPLEEV LNLAQSKNFHLRPRDLLISNINIVSVLELKGSETTFMCEYADETAT IVEFLNRWITFCQSI ISTLT |
| 339 | hIL-2 R38E/I92T | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTEM LTFKFYMPKKATELKH LQCLEEEELKPLEEV LNLAQSKNFHLRPRDLLISNINIVTVLELKGSETTFMCEYADETAT IVEFLNRWITFCQSI ISTLT |
| 340 | hIL-2 R38E/I92W | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTEM LTFKFYMPKKATELKH LQCLEEEELKPLEEV LNLAQSKNFHLRPRDLLISNINIVWVLELKGSETTFMCEYADETAT IVEFLNRWITFCQSI ISTLT |

TABLE 29-continued

| Sequences | | |
|-----------|--------------------------------------|--|
| SEQ ID | Name | Sequence |
| 341 | hIL-2 R38E/192Y | APTSSSTKKTQLQLEHLLLDLQMI LINGINNYKNPKLTEM LTFK F Y M P K K A T E L K H L Q C L E E E L K P L E E V LNLAQSKNFHLRPRDLISNINVVLELKGSETTFMCEYADETAT IVEFLNRWITFCQSI I STL T |
| 342 | hIL-2 R38E/192V | APTSSSTKKTQLQLEHLLLDLQMI LINGINNYKNPKLTEM LTFK F Y M P K K A T E L K H L Q C L E E E L K P L E E V LNLAQSKNFHLRPRDLISNINVVLELKGSETTFMCEYADETAT IVEFLNRWITFCQSI I STL T |
| 343 | hIL-2 R38E/H16E | APTSSSTKKTQLQLEHLLLDLQMI LINGINNYKNPKLTEM LTFK F Y M P K K A T E L K H L Q C L E E E L K P L E E V LNLAQSKNFHLRPRDLISNINVVLELKGSETTFMCEYADETAT IVEFLNRWITFCQSI I STL T |
| 344 | hIL-2 R38K/D20A | APTSSSTKKTQLQLEHLLLDLQMI LINGINNYKNPKLTEM LTFK F Y M P K K A T E L K H L Q C L E E E L K P L E E V LNLAQSKNFHLRPRDLISNINVVLELKGSETTFMCEYADETAT IVEFLNRWITFCQSI I STL T |
| 345 | WT hIL-2 | APTSSSTKKTQLQLEHLLLDLQMI LINGINNYKNPKLTEM LTFK F Y M P K K A T E L K H L Q C L E E E L K P L E E V LNLAQSKNFHLRPRDLISNINVVLELKGSETTFMCEYADETAT IVEFLNRWITFCQSI I STL T |
| 346 | Human PD-1 | PGWFLDSPDRPWPPTESPALLVVTGDNATFTCS ESNTSESFVLNWRMSPSNQTDKLAAPFEDRSQP GQDCRFRVTQLPNGRDFHMSVVRARRNDSGT Y L C G A I S L A P K A Q I K E S L R A E L R V T E R R A E V P T A H P S P SPRPAQGFQTLVVG V V G L L G S L V L L V V L A V I C S R A A R G T I G A R R T G Q P L K E D P S A V P V E S V D Y G E L D FQWREKTEPPVPVCPVEQTEYATI VFPSPGMGTS SPARRGSADGPRSAQPLRPEDGHC SWPL |
| 347 | Human PD-1 | CCAGGATGGTCTTAGACTCCCAGACAGGCCCTGGAACCCCCACCTTCTCCCAGCCCTGCTCGTG GTGACCGAAGGGGACAACGCCACCTTCACCTGCAGCTTCTCCAACACATCGGAGAGCTTCGTGCTAAAC TGGTACCGCATGAGCCCCAGCAACAGACGGACAAGCTGGCCGCCTTCCCGAGGACCGCAGCCAGCCC GGCCAGGACTGCCGCTTCCGTGTACACAACTGCCCAACGGGGCGTGACTTCCACATGAGCGTGGT CAGG GCCCGCGCAATGACAGCGGCACCTACCTCTGTGGGGCCATCTCCCTGGCCCCAAGGGCGAGATCAA GAGAGCTTCCGGCAGAGCTCAGGGTGACAGAGAGAAGGGCAGAAGTGCCCAAGCCACCCCGAGCCC TCACCAGGCCAGCCGGCCAGTCCAAACCCCTGGTGGTGGTGTGCTGGGGCGGCCGTGGCCAGCCGTG TGCTGTAGTCTGGGTCTGGCCGTGCATCTGCTCCCGGGCCGACAGGGGACAAATAGGAGCCAGGCGC ACCGGCCAGCCCCGTAAGGAGGACCCCTCAGCCGTGCCTGTGTTCTCTGTGGACTATGGGGAGCTGGAT TTCCAGTGGCGAGAGAAGACCCCGGAGCCCCCGTGCCTGTGCTCCCTGAGCAGACGGAGTATGCCACC ATGTCTTTCCTAGCGAATGGGCACCTCATCCCCGCGCCGAGGGGCTCAGCTGACGGCCCTCGGAGT GCCACGCACTGAGGCTGAGGATGGACACTGCTCTGGCCCCCTC |
| 348 | Anti-hPD-1 #1- mIgG2b-N297A HC | QVQLVESGGGVVQGRSLRLDCKASGITFSNSGMHWVRQAPGKGLEWVAVIWDGSKRYIADSVKGRFT ISRDN SKNTLFLQMNSLRAEDTAVYYCATNDDYWGQGLTVTVSSAKTTPPSVYPLAPGCGDITGSSVTL GCLVKGYFPPESTVTVNWSGSLSSVHTFPALLQSGLYTMSSSVTVPSSTWPSQTVTCSVAHPASSITVD KKLEP SGPISTINPCPPCKECHKCPAPNLEGGPSVFI FPPNI KDVLMI SLTPKVT CVVVDVSEDDPDVQ ISWFVNNVEVHTAQTQTHREDYASTIRVVS TLP IQHQDWMGSKKEFKCKVNNKDLPSPIERTISKI KGLV RAPQVYILPPPAEQLSRKDVSLTCLVVG ENPGDISVEWTSNGHTEENYKDTAPVLDSDGSYFIYSKLN KTSKWEKTD SFSCNVRHEGLKNYYLKKTI SRSPGK |
| 349 | Anti-hPD-1 #1- mKappa LC | EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRAITGIPARFSGSGSGT DFTLTISSELEPEDFAVYYCQSSSNWPRTPGQGTKEIKRADAAPT VSI FPPSSEQLTSGGASVVCBLNN FYPKDINVKWKIDGSEKQNGVLSWTDQDSKDSYSSMSSTLTLT KDEYERHNSYTC EATHKTSTSPIVK SENRNEC |
| 350 | Anti-hPD-1 #2- mIgG2b-N297A HC | QVQLVQSGVEVKKPGASVKVSKASGYTFNYYMYWVRQAPGQGLEWMMGGINPSNGGTNENEKEKNRVT LTTDSSTTAYMELKSLQFDITAVYYCARRDYRFDMGFDYWGQGLTVTVSSAKTTPPSVYPLAPGCGDT TGSVTLGCLVKGYFPPESTVTVNWSGSLSSVHTFPALLQSGLYTMSSSVTVPSSTWPSQTVTCSVAHP ASSTTVDKKLEP SGPISTINPCPPCKECHKCPAPNLEGGPSVFI FPPNI KDVLMI SLTPKVT CVVVDV SEDDPDVQISWFVNNVEVHTAQTQTHREDYASTIRVVS TLP IQHQDWMGSKKEFKCKVNNKDLPSPIERTI SKI KGLV RAPQVYILPPPAEQLSRKDVSLTCLVVG ENPGDISVEWTSNGHTEENYKDTAPVLDSDGSYF IYSKLNKMTSKWEKTD SFSCNVRHEGLKNYYLKKTI SRSPGK |
| 351 | Anti-hPD-1 #2- mKappa LC | EIVLTQSPATLSLSPGERATLSCRASKGVSTSGSYLHWYQQKPGQAPRLLIYLA SYLES GVPARESGS GSGTDFTLTISSELEPEDFAVYYCQHSRDLPLTFGGGTKEIKRADAAPT VSI FPPSSEQLTSGGASVVC FLMNFYPKDINVKWKIDGSEKQNGVLSWTDQDSKDSYSSMSSTLTLT KDEYERHNSYTC EATHKTSTSP IVKSENRENEC |
| 352 | IL-2RY | LNNTI LTPNGNEDTTADFFLTTPMPTDSLVSSTLPLPEVQCFVENVEYMNCTWNSSSEPQTNLTLHWY KNSDNDKVKCSHYLFS E E I T S G C Q L Q K K E I H L Y Q T F V V Q L Q D P R E P R Q A T Q M L K L Q N L V I P W A P E N L TLHKLSESOLELNNRFLNHCLEHLVQYRTDWDHWSWTEQSVDRHKESELPSVDGQKRYTERVRSREN LCGSAQHWS EWSHIPHWGNTSKENPFLFALEAVVIVSGSMGLIISLLCVYFWLERTMPRIPTLNKLED LVTEYHGNE SAWSGVSKGLAESLQPDYSERLCLVSEI PPKGGALGEGPGASPCNQHSPIYWAAPPCTYTLK ET |
| 353 | human CD122 (IL-2Rβ) | AVNGTSQFTCFYNSRANISCVWSQDQALQDTSQVHAWPDRRRWNQTC ELLPVSQASWACNLI LGAPDS QKLTTVDIVTLRVLCREGVRWRVMAIQDFKPFENLRMAPISLQVVHVE THR CNISWEISQASHYFERH LEFEARTLSPGHTWEEAPLLTLKQKQEWI CLETLTPDTQYEFQVRVKPLQGEFTTSPSPSPLAFRTK AALGKDTIPWLGHLVLSGAPGFIILVYLLINCRNTGPWLKVKLKNCTPDPSPKPSQLSSSEHGGDVQK WLSPPFPSSSESPGLAPEISPLEVLERDKVTQLLLQDQKVEPASLSNHSLSCTFTNQGYFFHFLPD ALEIEACQVYFTYDPSSEDDPEGVAGAPTGSSPQLPLQPLSGEDDAYCTFPSRDDLLLESPSLLGGPS PSTAPGSGAGEERMPPSLQERVPRDWDPPQLGPPTPGV PDLVDFQPPPELVLREAGEEVPDAGPREGV SFPWSRPPGQGEFRALNARLPLNTDAYLSLQELQGDPTHV |

TABLE 29-continued

| Sequences | | |
|------------|---|--|
| SEQ ID NO: | Name | Sequence |
| 370 | 1H3-hIgG1-L6-hCD25-L20-hIL-2 HC Linkers in dashed underline hIL-2 in italics | EVQLVESGGGLVQPGRSLKLSCAVSGFTFSDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGRET ISRDNAKITLYLQMDSLRSEDATATYYCARHSGSYFDYWGQGMVTVSSASTKGPSVFPPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPS NTKVDKKVEPKSCDKHTHTCPPELLEGGPSVLEFPPKPKDTLMI SRTPPEVTCVVVDVSHEDPEVKEN WYVDGVEVHNAKTKPREEQYNS TYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTI SKAKGQPR PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDK SRWQGNVVFSCVMHEALHNHYTQKSLSLSPGKSGGGGSELCDDDPPEI PHATFKAMAYKEGTMLNCEC KRGFRRIKSGSLYMLCTGNSSHSWQDQCCTSSATRNTTKQVTPQPEEQKERKTTTEMQSPMPVDQAS LPGHCREPPPWENEATERIYHFVVGQMVVYQCQVQGYRALHRGPAESVCKMTHGKTRWTQPQLICTSGGG GGGGGGGGGGGGGGGAPTSSSTKKTQLQLEHLLLDLQMLNNGINNYKNPKLTRMLTFKFPYMPKKATEL KHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLISNINIVLELKGSETTEMCEYADETATIVEFLNRWI TFCQSIISTLT |
| 371 | 1H3-hKappa-df-hCD25-L20-hIL-2 LC Linker in dashed underline hIL-2 in italics | DTVLTQSPALAVSPGERVTISCRASESVRTGVHWYQQKPGQPKLLIYGASNLESVGPAPRFSGSGSGTD FTLTIIDPVEADDTATYFCQQSWNDPFTFGSGTKLEIKRTVAAPSVEIFPPSDEQLKSGTASVVCLLNNE YPREAKVQWKVDNALQSGNSQESVTEQDSKDSSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSPVTKS FNRGCELCDDDDPPEI PHATFKAMAYKEGTMLNCECKRGERRIKSGSLYMLCTGNSSHSWQDQCCTSS SATRNTTKQVTPQPEEQKERKTTTEMQSPMPVDQASLPGHCREPPPWENEATERIYHFVVGQMVVYQCQ QGYRALHRGPAESVCKMTHGKTRWTQPQLICTSGGGGGGGGGGGGGGAPTSSSTKKTQLQLEHL LLDLQMLNNGINNYKNPKLTRMLTFKFPYMPKKATELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLI SNINIVLELKGSETTEMCEYADETATIVEFLNRWITFCQSIISTLT |
| 372 | 1H3-hKappa-L6-hCD25-L20-hIL-2 LC Linkers in dashed underline hIL-2 in italics | DTVLTQSPALAVSPGERVTISCRASESVRTGVHWYQQKPGQPKLLIYGASNLESVGPAPRFSGSGSGTD FTLTIIDPVEADDTATYFCQQSWNDPFTFGSGTKLEIKRTVAAPSVEIFPPSDEQLKSGTASVVCLLNNE YPREAKVQWKVDNALQSGNSQESVTEQDSKDSSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSPVTKS FNRGCELCDDDDPPEI PHATFKAMAYKEGTMLNCECKRGERRIKSGSLYMLCTGNSSHSWQDQCCTSS SATRNTTKQVTPQPEEQKERKTTTEMQSPMPVDQASLPGHCREPPPWENEATERIYHFVVGQMVVYQCQ QGYRALHRGPAESVCKMTHGKTRWTQPQLICTSGGGGGGGGGGGGGGAPTSSSTKKTQLQLEHL LQLEHLLLDLQMLNNGINNYKNPKLTRMLTFKFPYMPKKATELKHLQCLEEELKPLEEVLNLAQSKNEHL RPRDLISNINIVLELKGSETTEMCEYADETATIVEFLNRWITFCQSIISTLT |
| 373 | H7-02-hIgG4 HC | EVQLLESGGGLVQPGGSLRLSCAASGFTFKSYAMTVRQAPKKGLEWVSAIVYSGGSTYYADSVKGRGT ISRDNKNTLYLQMDSLRAEDTAVYYCAKYTRASYFYDAMDVWGQGTVTTVSSASTKGPSVFPPLAPCSR STSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYITC DHKPSNTKVDKRVESKYGPPCPPELLEGGPSVLEFPPKPKDTLMI SRTPPEVTCVVVDVSHEDPEVQ FNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSS IEKTI SKAKGQPR REPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTV DKSRWQEGNVVFSCVMHEALHNHYTQKSLSLSLGLG |
| 374 | 1H3-hkappa LC | DTVLTQSPALAVSPGERVTISCRASESVRTGVHWYQQKPGQPKLLIYGASNLESVGPAPRFSGSGSGTD FTLTIIDPVEADDTATYFCQQSWNDPFTFGSGTKLEIKRTVAAPSVEIFPPSDEQLKSGTASVVCLLNNE YPREAKVQWKVDNALQSGNSQESVTEQDSKDSSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSPVTKS FNRGCE |
| 375 | 2D12-mIgG1-D265A-L6-hIL-2 HC | EVQLQQSGPELVKPGASVKISCKTSGYTFTEYTMHWKQSHGKSLWEIIGGINPNNGGTTYNQKFKGKAT LTVDKSSSTAYMELRSLTQSDSAVYYCARDYRIGHYIYAMDYWGQGTSTVTVSSAKTTPPSVYPLAPGSA AQTNMVTLGCLVKGYFPEPVTVWNSGSLSSGVTFFPAVLQSDLYTLSSSVTVPSSTWPSSETVTCNVA HPASTKVDKIKVPRDCGCKPCICTVPEVSSVEIFPPKPKDVLTIITLTPKVT CVVVAISKDDPEVQESW FVDDDEVHTAQTPREEQFNSTFRSVSELPIMHQDWLNGKEPKCRVNSAAPPAPIEKTI SKTKGRPKAP QVYTI PPPKEQMAKDKVSLT CMITDFPEDI TVEWQWNGQPAENYKNTQPIMDTDGSYFVYSKLNQKS NWEAGNTFTCSVLHEGLHNHTEKSLSHSPGKSGGGGAPTSSSTKKTQLQLEHLLLDLQMLNNGINNY KNPKLTRMLTFKFPYMPKKATELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLISNINIVLELKGSE TTFMCEYADETATIVEFLNRWITFCQSIISTLT |
| 376 | 2D12-mkappa LC | QIVLTQSPAIMASAPGKVTMTCSVSSVREMHWYQQKSGTSPKRWIYDTSKLSGVPAPRFSGSGSGTS YSLTISSEAEADAATYFCQQSWNDPFTFGGKTKLEIKRADAAPTVEIFPPSDEQLTSGGASVFCPLNNE YPKIDINVKWKIDGSEKQGNVLSWTDQDSKDSSTYSMSSTLTITKDEYERHNSYTCETHKSTSPVKS FNRNEC |
| 377 | hIL-2 Q126L | APTSSSTKKTQLQLEHLLLDLQMLNNGINNYKNPKLTRMLTFKFPYMPKKATELKHLQCLEEELKPLEEVL LNLAQSKNFHLRPRDLISNINIVLELKGSETTEMCEYADETATIVEFLNRWITFCLSIISTLT |
| 378 | hIL-2 Q126E | APTSSSTKKTQLQLEHLLLDLQMLNNGINNYKNPKLTRMLTFKFPYMPKKATELKHLQCLEEELKPLEEVL LNLAQSKNFHLRPRDLISNINIVLELKGSETTFMCEYADETATIVEFLNRWITFCESIISTLT |
| 379 | 1H3-hIgG1 HC | EVQLVESGGGLVQPGRSLKLSCAVSGFTFSDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGRFT ISRDNAKITLYLQMDSLRSEDATATYYCARHSGSYFDYWGQGMVTVSSASTKGPSVFPPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPS NTKVDKKVEPKSCDKHTHTCPPELLEGGPSVLEFPPKPKDTLMI SRTPPEVTCVVVDVSHEDPEVKEN |

TABLE 29-continued

| Sequences | | |
|------------|-------------------------|---|
| SEQ ID NO: | Name | Sequence |
| | | WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPRE PQVYITLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDK SRWQQGNVFSQSVMEALHNHYTQKLSLSLSPGK |
| 380 | huPD-1-Fc | MQIQAPWPVAVLQGLGWRPGWELDSPDRPWNPPTESPALLVVTGDNATFTCSSENTSESVLWNWYR MSPSNQTDKLAAPFEDRSQPGQDCRFVTLQPNGRDFHMSVVRARRNDSGTYLCGAI SLAPKAQIKESL RAELRVTERRAEVPTAHPSPSPRPAQGFQIEGRMDPKSCDKTHTCPPCPAPELGGPSVLEFPPPKPDT LMI SRTPVETCVVVDVSHEDPEVKENWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYITLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVMEALHNHYTQKLSLSLSPGK |
| 381 | cynomolgous- PD-1-Fc | MQIQAPWPVAVLQGLGWRPGWFLESPPDRPWNAPTFSPALLLVTEGDNATFTCSFSNASESVLWNWYR MSPSNQTDKLAAPFEDRSQPGQDCRERVTRLNGRDFHMSVVRARRNDSGTYLCGAI SLAPKAQIKESL RAELRVTERRAEVPTAHPSPSPRPAQGFQIEGRMDPKSCDKTHTCPPCPAPELGGPSVLEFPPPKPDT LMI SRTPVETCVVVDVSHEDPEVKENWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYITLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSQSVMEALHNHYTQKLSLSLSPGK |
| 382 | 2H7 VH | GAGGTGCAGCTGCTGGAAAGCGGCGGACTGGTGCAGCCTGGAGGCAGCCTGCGGCTGTCTGTGCC GCTTCTGGCTTACCTTCAAGGACTACTGCATGACCTGGGTGACAGCAGGCCCTGGCAAGGCCCTCGAG TGGGTGTCCGCCATCGTGTACAGCGCGGGTCAACATACTACGCCGACAGCCTGAAGGGCAGATTACA ATCAGCAGAGATAACAGCAAGAACCCTGTACCTGCAGATGAACAACCTGAGAGCTGAAGATACCGCC GTGTACTACTGCGCCAAGTACACCAGAGCCAGTACTTCTACGACGCCATGGACGTGGGGCCAGGGC ACCACCGTGACAGTGTCTCAT |
| 383 | 2H7 VL | GAGATCGTGCTGACCCAGTCTCCTGGCACCTGAGCCTGAGCCTGGCGAGAGACTACTGTCATGC AGAGCCTCTCAGAGCATCGGCAAGACTTCTGGCCTGGTACAGCAAAAGCCTGGACAGGCCCTTAGA CTGCTGATCTACGACGCCAGCACCAGAGCCGCTGATATCCCCCAGATTACAGCGGATCTGGCAGCGGC ACTGATTTCAACCTCACCATCAGCAGCCTGGAACCGAGGACTTCGCCGTGTACTACTGCCAGCAGTAC TAGACTGGCCCCCTGTCTTTTGGCGGAGGCACAAAGGTGAAATCAAG |
| 384 | 2H7 VH | EVQLLESQGLVQPGGSLRLSCAASGFTFKDYCMTWVRQAPGKLEWVSAIVYSGGSTYYADSVKGRFT ISRDNKNTLYLQMNRLRAEDTAVYYCAKYTRASYFYDAMDVWGQTTVTVSS |
| 385 | 2H7 VL | EIVLTQSPGTLSPGERATLSCRASQSIGKSFLLAWYQQKPGQAPRLLIYDASTRAADI PARFSGSGSG TDFTLTISSLEPEDFAVYYCQQYDWPPLSFGGGTKVEIK |
| 386 | 2H7 HCDR1 | GFTFKDYCMT |
| 387 | 2H7 HCDR2 | AIVYSGGSTYYADSVKG |
| 388 | 2H7 HCDR3 | YTRASIFYDAMDV |
| 389 | 2H7 LCDR1 | RASQSIGKSFLLA |
| 390 | 2H7 LCDR2 | DASTRAA |
| 391 | 2H7 LCDR3 | QQYDWPPLS |
| 392 | C51E6-5 VH | CAGGTTGAGCTGGTTCAGTCTGGCAGCAGCTGAAGAAACCTGGCGCCTCTGTGAAGGTGCTCTGCAAG GCCCTGGCTACAGCCTGTACGGCAGCTCTATGCACTGGGTCCGACAGCCTCCAGGACAGGGACTTGG TGGATGGGCTACATCAGCCCTTTACCGGAGAGCCACATACGCCAGGGCTTCACAGGCAGATTCTGT TTCAGCCTGGACACCAGCGTGTCCACAGCCTACCTGCAGATCAGTCTCTGAAGGCCGAGGACACCGCC GTGTACTACTGCGCCAGAGACTACGACTACCGGTACTACTATGCCATGGACTACTGGGCGCAGGGCACC ACAGTTACAGTGTCTCA |
| 393 | C51E6-5 VL | GAAATGTGCTGACACAGAGCCCGACTTCCAGAGCGTGACCCCTAAAGAAAAGTGACCATCACCTGT ACCGCCAGCGAGTCCGTGCCCTCCTCAGTTCCTGCAATGGTATCAGCAGAAGCCGATCAGAGCCCCAAG CTGCTGATCTACGCCAGCAGAGAAAGAGCCAGCGGCTCCCAAGCAGATTTCTGGCTCTGGCAGCGGC ACCGACTTCAACCTGACAATCAATAGCCTGGAAGCCGAGGACGCCGCCACCTACTACTGCCACAGTTT CACAGAAGCCCTTGACCTTTGGCGGAGGCACCAAGCTGGAATCAAG |
| 394 | C51E6-5 VH | QVQLVQSGSELKPKGASVKVSKASGYSLYGTSMHWRQAPGQGLEWVMYISPFTRGRATYAQGFTGRFV FSLDTSVSTAYLQISSLKAEDTAVYYCARDYDYYRYYYAMDYWGQTTVTVSS |
| 395 | C51E6-5 VL | EIVLTQSPDFQSVTPKEKVTITCTASESVPPQFLHWYQQKPDQSPKLLIYASFRERASGVPSRESGSGSG TDFTLTINSLAEDAATYYCHQFHRSPFTFGGGTKLEIK |
| 396 | C51E6-5 HCDR1 | GYSLYGTSMH |
| 397 | C51E6-5 HCDR2 | YISPFTRGRATYAQFTG |
| 398 | C51E6-5 HCDR3 | DYDYRYYYAMDY |
| 399 | C51E6-5 LCDR1 | TASESVPPQFLH |

TABLE 29-continued

| Sequences | | |
|------------|----------------------------|---|
| SEQ ID NO: | Name | Sequence |
| 400 | C51E6-5 LCDR2 | ASRERAS |
| 401 | C51E6-5 LCDR3 | HQFHRSPLT |
| 402 | A2 VH | GACGTGCAGCTGGTGGAAAGCGGCGGAGGCTGGTCCAGCCCGCGGCTCTCTGAGACTGAGCTGCGCC GCCAGCGGCTTACCTTCGACATCAGCGCCATGAGCTGGGTGCGGCAGGCCCTGGCAAGGGCCTGGAA TGGGTGAGCACAATCAGCGGATCTGCCTACAGCACCTACTACGCCGACAGCGTGAAGGGCAGATTACCC ATCTCAAGAGATAACAGCAAGAGCACCCCTGTACCTGCAGATGAACAGCCTGCGGGCCGAGGACACCGCC GTGTACTACTGCGCCAGAGAGATCTTCAGCGACTACTGGGGCTTGGGCACCCCTGGTGACAGTGTCTCTCA |
| 403 | A2 VL | CAAAGCGTGTGACACAGCCCCAGCGCTTCTGGCACCCCTGGCCAGAGAGTGACCATCTCATGAGC GGGTCAACAAGCAACATCGGCAGAGAGCGTGTACTGGTACCAGCAGCTGCCTGGAAACCGCCCCAAG CTGCTGATCTACAGCAACGTGCAGCGGCTAGCGGCGCCCTAACAGATTACGCGGACAGCAAGAGCGGC ACCAGCGCCAGCCTGGCCATCAGCGGCTGCAGAGCGAGGACGAGGCCGACTACTACTGCGGCACATGG GACGACAGCCTGAACGGCTGGGTGTTTCGCGCGCGGAACTAAGCTGACCCGTCCTA |
| 404 | A2 VH | DVQLVESGGGLVQPGGSLRLSCAASGFTFDISAMSWVRQAPGKLEWVSTISGSAYSTYYADSVKGRFT ISRDNKSTLYLQMNLSRAEDTAVYYCAREIFSDYWGLGLTVTVSS |
| 405 | A2 VL (OMC479p1 . A2VL) | QSVLTQPPASGTPGQRVTISCSGSTSNIGRESVYVYQQLPGTAPKLLIYSNVQRPSGAPNRESGSKSG TSASLAIISGLQSEDEADYYCTWDDSLNGWVFGGGTKLTVL |
| 406 | A2 HCDR1 | GFTFDISAMS |
| 407 | A2 HCDR2 | TISGSAYSTYYADSVKQ |
| 408 | A2 HCDR3 | EIFSDY |
| 409 | A2 LCDR1 | SGSTSNIGRESVY |
| 410 | A2 LCDR2 | SNVQRPS |
| 411 | A2 LCDR3 | GTWDDSLNGWV |
| 412 | H7-767 HC | GAGGTGCAGCTGCTGGAAAGCGGCGGCGGCTCGTGCAGCCTGGCGGATCTCTGCGGCTGAGCTGTGCT GCCAGCGGCTTACATTTAAATCCTACGCCATGCACTGGGTAGACAAGCCCGGAAAGGGCCTGGAA TGGGTGTCCGCATCGCTACAGCGCGGATCTACATACTACGCCGACAGCGTGAAGGGCCGGTTACC ATCAGCAGAGATAATAGCAAGAACCCTGTACCTGCAGATGAACAGCCTGAGAGCCGAGGACACCGCC GTGTACTACTGCGCCAAGTACGACAGAGCTTCTTATTCTACGATGCCATGGACGTGTGGGGCCAGGGC ACCACCGTGACAGTGTCTCAGCTAGCACCAAGGGCCCTAGCGTGTTCACACTGGCCCCCTAGCTCTAAA AGCACAAAGCGGCGGAACCCGCGCTCTGGTGTCTGGTGAAGGACTACTTCCCTGAGCCTGTGACCGCT AGCTGGAACAGCGGCGCCCTGACCAGCGGCTTCAACATTCCTCCGCTGTGTCAGAGCTCTGGGCTG TACAGCCTGAGCAGCGTGGTACCGTGCCTTCTTCTCTGGGCACACAAACATACATCTGCAACGTG AACCAACAGCCAGTAATACCAAGTGGATAAGAAGGTGGAACCTAAGTCTTTCGACAAAGCCACACC TGCTCCCGTGCCCTGCTCCTGAACTGgetGGagetCCCAGCGTGTTCCTGTTCCTCCCAAACTAAA AGCACCTGATGATCAGCCGGAACCCCTGAGGTGACCTGCGTGGTGTGTCGACGTGTCCACGAAATCCT GAGGTGAAGTTCAACTGGTACGTGGAACCGGCTGGAAGTGCATRAATGCCAAGCAAAGCTAGAGAGGAA CAGTACAACAGCACCTATAGAGTGGTGTCCGTGCTGACAGTGTCTGACAGGACTGGCTGAACGGCAAG GAATACAAGTGAAGGTGTCACAAAGGCCCTCCCGCCCTATCGAGAAGACCATCAGCAAGGCCAAG GGCCAACTAGAGAGCCCGAGGTGTACACCTGCCCTCAAGCAGAGATGAGCTGACCAAGAACCAGGTT AGCCTGACTTGTCTGGTGAAGGCTTCTACCCCTCCGATATCGCCGTGGAATGGGAGAGCAACGGCCAG CCTGAGAACAACACTACAAGACCACCTCCAGTGTGGACAGCGGACCGGAGCTTCTTCTGTATAGCAAG CTGACAGTGGACAAGAGCAGATGGCAGCAGGGCAACGTGTTTACGTGACAGCTCATGACAGGCCCCCTG CACAACTTACACCCAGAACTCTGAGCTGAGCCCTGGAAGGCCCTGCTTCTAGCAGCACCAAG AAGACCCAGCTGACGTGGAACACCTGTGCTGGCCCTGCAGATGATCCTGAACGGCATCAACAACACTAC AAGAACCCTAAGCTGACCGAGATGCTGACATTTAAGTCTACATGCTAAGAAGCCACCGAGCTGAAG CACCTGCAATGTCTGGAAGAAGAGCTGAAACCTCTGGAAGAGGTGCTGAATCTGGCTCAGTCAAAGAAC TTCCACCTTAGACCTAGAGATCTGATCAGCAACATCAACGTGATCGTGTGGAACGAAAGGCGAGCGAG ACGACCTTACATGTGCGAGTACGCCGACGAGCAGCCACAATCGTGGAGTTCCTGAACAGATGGATCACC TTGCCCCAGAGCATCATCTCCACCTGACC |
| 413 | H7-767 LC | GAGATCGTGTGACCCAGTCCCAGGCACACTGAGCCTGAGCCCCGGCGAGCGGGCCACCTGAGCTGT AGAGCTAGCCAGAGCATCTCCAGCAGCTTCTGGCCCTGGTACCAGCAGAAACCTGGCCAGGCCCTAGA CTGCTGATCTACGACGCCCTCTGATAGAGCTACAGGCATCCCCGACCGGTTACAGCGGACGCGGATCTGGC ACCGACTTACCCCTGACCATCAGCAGACTCGAGCCTGAAGATTTCCGCGTGTACTACTGCCAGCAATAC TATGACTGGCCCTCTCTGTCTTTGGCGGCGGAACAAGGTGGAAATTAAGCGTACGGTGGCGGCCCC AGCGTGTTCATCTTCCACCCAGCAGCAGCAGCTGAAGTCCGGCACAGCCAGCGTGGTGTGCTGCTG AACAACTTCTACCCCGCAGGCAAGGTGACGTGGAAGGTGACCAACGCCCTGCAGAGCGGCAACAGC CAGGAAAGCGTGACCGAGCAGGACAGCAAGGACTCCACCTACAGCCTGAGCAGCACCTGACCCCTGAGC AAGGCCGACTACGAGAAGCACAAAGGTGTACGCCCTGCGAAGTGACCCACAGGCGCTGTCCAGCCCTGT ACCAAGAGCTTCAACCGGGCGGAGTGC |

TABLE 29-continued

| Sequences | | |
|------------|----------------------|--|
| SEQ ID NO: | Name | Sequence |
| 414 | H7-632 HC CDRs solid | EVQLLESGGGLVQPGGSLRLSCAASGFTFKSYAMHWVRQAPGKLEWVSAIVYSGGSTYYADSVKGRFT ISRDNSKNTLYLQMNSLRAEDTAVYYCAKYDRASYFYDAMDVWGQGT ^T TVTVSSASTKGPSVFFLAPSSK |
| | underlined | <u>STSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYICNV</u> |
| | Constant | <u>NHKPSNTKVDKRVESKYGPPCPPAPEFLGGPSVFLPPPKPDTLMI</u> SRTPEVTCVVVDVSDVQEDPEVQ |
| | region dashed | <u>EVKFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI</u> SKAKQP |
| | underlined | <u>REPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSLR</u> <u>LTVDKSRWQEGNVFSCVMHEALHNHYTQKSLSLSPG</u> |
| 415 | H7-632 LC CDRs solid | EIVLTQSPGTLSLSPGERATLSCRASQSISSSFLAWYQQKPGQAPRLLIYDASDRATGIPDRESGSGS TDFTLTISRLEPEDFAVYYCQQYYDWPPLSF ^G GGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL |
| | underlined | <u>NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDS</u> TYLSSTLTLSKADYEKHKVYACEVTHQGLSPV |
| | Constant | <u>KSRWQEGNVFSCVMHEALHNHYTQKSLSL</u> SLGKSGGGGSAPTSSSTKKTQLQLEHLLALQMLNGLN |
| | region dashed | <u>EVKFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI</u> SKAKQP |
| | underlined | <u>REPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSLR</u> <u>LTVDKSRWQEGNVFSCVMHEALHNHYTQKSLSLSPG</u> |
| 416 | H7-632 VH | EVQLLESGGGLVQPGGSLRLSCAASGFTFKSYAMHWVRQAPGKLEWVSAIVYSGGSTYYADSVKGRFT ISRDNSKNTLYLQMNSLRAEDTAVYYCAKYDRASYFYDAMDVWGQGT ^T TVTVSS |
| 417 | H7-632 VL | EIVLTQSPGTLSLSPGERATLSCRASQSISSSFLAWYQQKPGQAPRLLIYDASDRATGIPDRESGSGS TDFTLTISRLEPEDFAVYYCQQYYDWPPLSF ^G GGTKVEIK |
| 418 | H7-632 HCDR1 | GFTFKSYAMH |
| 419 | H7-632 HCDR2 | AIVYSGGSTYYADSVK |
| 420 | H7-632 HCDR3 | YDRASYFYDAMDV |
| 421 | H7-632 LCDR1 | RASQSISSSFLA |
| 422 | H7-632 LCDR2 | DASDRAT |
| 423 | H7-632 LCDR3 | QQYYDWPPLS |
| 424 | 2H7-hIgG4 HC | EVQLLESGGGLVQPGGSLRLSCAASGFTFKDYCMTWVRQAPGKLEWVSAIVYSGGSTYYADSVKGRFT ISRDNSKNTLYLQMNLR ^A EDTAVYYCAKYTRASYFYDAMDVWGQGT ^T TVTVSSASTKGPSVVEPLAPCSR STSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTKTYTCNV DHKPSNTKVDKRVESKYGPPCPPAPEFLGGPSVFLPPPKPDTLMISRTPEVTCVVVDVSDVQEDPEVQ FNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKQP REPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSLR LTDKSRWQEGNVFSCVMHEALHNHYTQKSLSLSLG |
| 425 | 2H7-hkappa LC | EIVLTQSPGTLSLSPGERATLSCRASQSI ^G KSFLAWYQQKPGQAPRLLIYDASTRAADI ^P ARESGSGS TDFTLTISRLEPEDFAVYYCQQYYDWPPLSF ^G GGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYLSSTLTLSKADYEKHKVYACEVTHQGLSPV TKSENREGC |
| 426 | C51E6-5-hIgG4 HC | QVQLVQSGSELKPKGASVKVSKASGYSLYGTSMHWVRQAPGQLEWGMGYS ^P PFTGRATYAQGTGREV FSLDTSVSTAYLQISSLKAEDTAVYYCARDYDYRYYYAMDYWGQGT ^T TVTVSSASTKGPSVVEPLAPCSR TSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTKTYTCNV HKPSNTKVDKRVESKYGPPCPPAPEFLGGPSVFLPPPKPDTLMISRTPEVTCVVVDVSDVQEDPEVQ FNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKQP REPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSLR LTDKSRWQEGNVFSCVMHEALHNHYTQKSLSLSLG |
| 427 | C51E6-5-hKappa LC | EIVLTQSPDFQSVTPKEKVTITCTASESVPPQFLHWYQQKPDQSPKLLIYASRERASGVPSRESGSGS TDFTLTINSLEAEDAATY ^C HQPHRSPLTFGGGKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLN NFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYLSSTLTLSKADYEKHKVYACEVTHQGLSPV KSENREGC |
| 428 | A2-hIgG4 HC | DVQLVESGGGLVQPGGSLRLSCAASGFTFDISAMSWVRQAPGKLEWVSTISGSAYSTYYADSVKGRFT ISRDNSKNTLYLQMNSLRAEDTAVYYCAREIFSDYWGGLGLVTVSSASTKGPSVFFLAPCSRSTSESTA ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTKTYTCNV DHKPSNTKVDKRVESKYGPPCPPAPEFLGGPSVFLPPPKPDTLMISRTPEVTCVVVDVSDVQEDPEVQ FNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKQP REPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSLR LTDKSRWQEGNVFSCVMHEALHNHYTQKSLSLSLG |

TABLE 29-continued

| Sequences | | |
|------------|---|---|
| SEQ ID NO: | Name | Sequence |
| 429 | A2-hLambda LC | QSVLTQPPSASGTPGQRVITISCSGSTSNI GRESVYVYQQLPGTAPKLLIYSNVQRPSGAPNRESGSKSG TSASLAI SGLQS EDEADYICGTWDDSLNGWVFGGGTKLTVLGGPKAAPSVTLEPPSSEELQANKATLVC LISDFYPGAVTVAWKADSSPVKAGVETTPPKSQSNKYAASSYLSLTPQEWKSHRSYSCQVTHEGSTVE KTVAPTECS |
| 430 | 2H7-hIgG4-df-hIL-2 (D20A/R38E) HC hIL-2 in italics | EVQLLES GGGLVQPGGSLR LSCAASGFTFKDYCMTWVRQAPGKGLEWVSAIVYSGGSTYADSVKGRFT ISRDN SKNTLYLQMN NLR AEDTAVYYCAKYTRASYFYDAMDVWGQGT TTVTVSSASTKGPSVFP LAPCSR STSESTAALGCLVKDYFPEPVTVSWNSGALTS GVHTFPAVLQSSGLYSLS SVVTVPSSSLGTKTYTCNV DHKPSNTKVDKRVESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQ FNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQP REPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSPFLYSRLTV DKSRWQEGNVFSCSVMEALHNHYTQKLSLSLGKAPTSSSTKKTQLQLEHLLALQMI LNGINNYKNP KLTEMLTFK FYPMPK KATEL KHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLI SNINVI VLELKGSETTE MCEYADETAT IVEFLNRWITFCQSIISTLT |
| 431 | H7-632-hIgG1-LAGA-df-hIL-2 (T3A/C125A) HC | EVQLLES GGGLVQPGGSLR LSCAASGFTFKSYAMHWVRQAPGKGLEWVSAIVYSGGSTYADSVKGRFT ISRDN SKNTLYLQMN NLR AEDTAVYYCAKYDRASYFYDAMDVWGQGT TTVTVSSASTKGPSVFP LAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTS GVHTFPAVLQSSGLYSLS SVVTVPSSSLGTKTYTCNV NPKPSNTKVDKRVESKYGPPCPPAPELAGAPSVFLFPPKPKDTIMISRTPEVTCVVVDVSDQEDPEVQ FNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI SKAK GQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSPFLYSK LTVDKSRWQEGNVFSCSVMEALHNHYTQKLSLSLPGKAPASSTKKTQLQLEHLLALQMI INGINNY KPKLTRMLTFK FYPMPK KATEL KHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLI SNINVI VLELKGSE ITEMCEYADETAT IVEFLNRWITFAQSIISTLT |
| 432 | C51E6-5-hIgG4-L6-hIL-2 (D20A/R38E) HC Linker in dashed underline hIL-2 in italics | QVQLVQSGSELKKPGASVKVSCASGYSLYGTSMHWVRQAPGQGLEWVMGYISPFTRATYAGQGTGRFV FSLDTSVSTAYLQISSLKAEDTAVYYCARDYDRIYRYAMDYWGQGT TTVTVSSASTKGPSVFP LAPCSR TSESTAALGCLVKDYFPEPVTVSWNSGALTS GVHTFPAVLQSSGLYSLS SVVTVPSSSLGTKTYTCNV HKPSNTKVDKRVESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQ FNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQP REPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSPFLYSRLTV DKSRWQEGNVFSCSVMEALHNHYTQKLSLSLGKSGGGGSAPTSSSTKKTQLQLEHLLALQMI LNGIN NYKPKLTEMLTFK FYPMPK KATEL KHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLI SNINVI VLELKG SETTEMCEYADETAT IVEFLNRWITFCQSIISTLT |
| 433 | A2-hIgG4-df-hIL-2 (D20A/R38E) HC hIL-2 in italics | DVQLVESGGGLVQPGGSLR LSCAASGFTFDISAMSWVRQAPGKGLEWVSTISGSAYSTYADSVKGRFT ISRDN SKSTLYLQMN NLR AEDTAVYYCAREIFSDYWGGLTVTVSSASTKGPSVFP LAPCSRSTSESTA ALGCLVKDYFPEPVTVSWNSGALTS GVHTFPAVLQSSGLYSLS SVVTVPSSSLGTKTYTCNVDHKPSNT KVDKRVESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWYVDG VEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQP REPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSPFLYSRLTV DKSRWQEGNVFSCSVMEALHNHYTQKLSLSLGKAPTSSSTKKTQLQLEHLLALQMI LNGINNYKPKL TEMLTFK FYPMPK KATEL KHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLI SNINVI VLELKGSETTE MCEYADETAT IVEFLNRWITFCQSIISTLT |
| 434 | 1H3-hIgG4-df-hIL-2 (D20A/R38E) HC hIL-2 in italics | EVQLVESGGGLVQPGSLKLSCAVSGFTFDYAMAWVRQAPKKGLEWVATISYDGSRTYRDSVKGRE ISRDN AKITLYLQMN NLR AEDTAVYYCARHSGYFDYWGQVMVTVSSASTKGPSVFP LAPCSRSTSE TAALGCLVKDYFPEPVTVSWNSGALTS GVHTFPAVLQSSGLYSLS SVVTVPSSSLGTKTYTCNV DHKPSNTKVDKRVESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQ FNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQP REPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSPFLYSRLTV DKSRWQEGNVFSCSVMEALHNHYTQKLSLSLGKAPTSSSTKKTQLQLEHLLALQMI LNGINNYKPKL TEMLTFK FYPMPK KATEL KHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLI SNINVI VLELKGSETTE MCEYADETAT IVEFLNRWITFCQSIISTLT |
| 435 | 2H7-hIgG4-df-hIL-2 (T3A/D20A/R38E/C125A) HC hIL-2 in italics | EVQLLES GGGLVQPGGSLR LSCAASGFTFKDYCMTWVRQAPGKGLEWVSAIVYSGGSTYADSVKGRFT ISRDN SKNTLYLQMN NLR AEDTAVYYCAKYTRASYFYDAMDVWGQGT TTVTVSSASTKGPSVFP LAPCSR STSESTAALGCLVKDYFPEPVTVSWNSGALTS GVHTFPAVLQSSGLYSLS SVVTVPSSSLGTKTYTCNV DHKPSNTKVDKRVESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQ FNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQP REPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSPFLYSRLTV DKSRWQEGNVFSCSVMEALHNHYTQKLSLSLGKAPASSTKKTQLQLEHLLALQMI LNGINNYKPKL TEMLTFK FYPMPK KATEL KHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLI SNINVI VLELKGSETTE MCEYADETAT IVEFLNRWITFAQSIISTLT |
| 436 | hPD-1 extracellular domain | CCAGGATGGTCTTAGACTCCCAGACAGGCCCTGGAAACCCCCACCTTCTCCCAGCCCTGCTCGTG GTGACCGAAGGGGACAAACCCACCTTCACTCGAGCTTCTCCAACACATCGGAGAGCTTCGTGCTAAAC TGGTACCGCATGAGCCCAGCAACAGACGGACAAGCTGGCCGCTTCCCAGGACCCGACGCCCC GGCCAGGACTGCCCTTCCGTGTACACAACAGTCCCAACGGCGTGACTTCCACATGAGCGTGGTCAGG GCCCGCGCAATGACAGCGGCATCCTCTGTGGGGCCATCTCCCTGGCCCCAAGGCGCAGATCAA GAGAGCCTGCGGGCAGAGCTCAGGTCAGACAGAGAGAGGGCAGAAAGTGCACAGCCACCCAGCCCC TCACCAGCCAGCCGCGCAGTCCAA |

TABLE 29-continued

| Sequences | | |
|------------|----------------------------------|--|
| SEQ ID NO: | Name | Sequence |
| 437 | hPD-1 extracellular domain HC | PGWFLDSPDRPWNPPTFSPALLVVTEGDNATFTCSFSNTSESFVLNWRMSPSNQTDKLAAPFEDRSQP GQDCRFVTVQLPNGRDFHMSVVRARRNDSGTYLCAISLAPKAQIKESLRAELRVTERAEVPTAHPSP SPRPAQQFQ |
| 438 | OMC . 1. B6-hIgG4 HC | EVQLLESGGGLVQPGGSLRLSCAASGFTESSNYMSWVRQAPGKLEWVSAISSGGTIFYADSVKGRFT ISRDNKNTLYLQMNSLRAEDTAVYYCAKHKWNAVYYDGMVWVGQTTVTVSASATKGPSVFPPLAPCSR STSESTAALGCLVKDYFPEPVTVSWNSGALTSQVHTFPAVLQSSGLYSLSSVTVTPSSSLGKTKYTCNV DHKPSNTKVDKRVESKYGPPCPPEPEFLGGPSVFLFPPKPKDTLMI SRTP EVT CVVVDVSDQEDPEVQ FNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQP REPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTV DKSRWQEGNVFSCVMHEALHNHYTQKSLSLSLG |
| 439 | OMC . 1. B6-hLambda LC | QSVLTQPPASGTPGQRVTISCSGSNSNI GRNLVNWYQQLPGTAPKLLIYTI DQRPSGVPDRESGSKSG TSASLVI SGLQSEDEADYYCAAWDGLNANWVFGGGTKLTVLGQPKAAPSVTLLEPPSSEELQANKATLVC LISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNKYAASSYLSLTPEQWKS HRYSYSCQVTHEGSTVE KTVAPTECS |
| 440 | OMC . 2. C6-hIgG4 HC | EVQLLESGGGLVQPGGSLRLSCTASGFTESSEYEMQWVRQAPGKLEWVGLITSSSSHIFYADSVKGRFT VSRDNKNTLYLQMNSLRAEDTAVYYCTKDLNSYYGLDVWVGQTTVTVSSASATKGPSVFPPLAPCSRST ESTAALGCLVKDYFPEPVTVSWNSGALTSQVHTFPAVLQSSGLYSLSSVTVTPSSSLGKTKYTCNV PSNTKVDKRVESKYGPPCPPEPEFLGGPSVFLFPPKPKDTLMI SRTP EVT CVVVDVSDQEDPEVQENW YVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQP QVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKS RWQEGNVFSCVMHEALHNHYTQKSLSLSLG |
| 441 | OMC . 2. C6-hLambda LC | QSVMTQPPASGTPGQRVTISCSGSSTNLGNVSWYQHLPGTAPKLLIYGN DQRPSGVPDRESGSKSG TSASLAI SGLQSDDEADYYCSDWASLNWVWVFGGGTKLTVLGQPKAAPSVTLLEPPSSEELQANKATLVC LISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNKYAASSYLSLTPEQWKS HRYSYSCQVTHEGSTVE KTVAPTECS |
| 442 | OMC . 1. D6-hIgG4 HC | EVQLLESGGGLVQPGGSLRLSCAASGFTFSDYYMSWVRQAPGKLEWVSAISSGGTIFYADSVKGRFI ISRDNKNTLYLQMNSLRAEDTAVYYCAKHKWNDVYDAMDVWVGQTTVTVSASATKGPSVFPPLAPCSR STSESTAALGCLVKDYFPEPVTVSWNSGALTSQVHTFPAVLQSSGLYSLSSVTVTPSSSLGKTKYTCNV DHKPSNTKVDKRVESKYGPPCPPEPEFLGGPSVFLFPPKPKDTLMI SRTP EVT CVVVDVSDQEDPEVQ FNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQP REPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTV DKSRWQEGNVFSCVMHEALHNHYTQKSLSLSLG |
| 443 | OMC . 1. D6-hLambda LC | QSVLTQPPASGTPGQRVTISCSGSNSNI GRNLVNWYQQLPGTAPKLLIYTV DQRPSGVPDRESGSKSG TSASLAI SGLQSEDEADYYCAAWDSSLNWSVFGGGTKLTVLGQPKAAPSVTLLEPPSSEELQANKATLVC LISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNKYAASSYLSLTPEQWKS HRYSYSCQVTHEGSTVE KTVAPTECS |
| 444 | D12-hIgG4 HC | DVQLVESGGGLVQPGGSLRLSCAASGFTFDISAMSWVRQAPGKLEWVSTISGSAYSTYYADSVKGRFT ISRDNKSTLYLQMNSLRAEDTAVYYCAREIFSDYWGLGTLVTVSSASATKGPSVFPPLAPCSRSTSESTA ALGCLVKDYFPEPVTVSWNSGALTSQVHTFPAVLQSSGLYSLSSVTVTPSSSLGKTKYTCNV KVDKRVESKYGPPCPPEPEFLGGPSVFLFPPKPKDTLMI SRTP EVT CVVVDVSDQEDPEVQFNWYVDG VEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQP REPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTV DKSRWQEGNVFSCVMHEALHNHYTQKSLSLSLG |
| 445 | D12-hLambda LC | QSVLTQPPASGTPGQRVTISCSGNTSNI GRESVYVYQQLPGTAPKLLIY SNVQRPSGVPDRESGSKSG TSASLAI SGLQSEDEADYYCGTWDDSLNGWVFGGGTKLTVLGQPKAAPSVTLLEPPSSEELQANKATLVC LISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNKYAASSYLSLTPEQWKS HRYSYSCQVTHEGSTVE KTVAPTECS |
| 446 | G12-hIgG4 HC | DSLVESGGGLVQPGGSLRLSCAASGFTFDISAMSWVRQAPGKLEWVSTISGSAYSTYYADSVKGRFTI SRDNKSTLYLQMNSLRAEDTAVYYCAREIFSDYWGLGTLVTVSSASATKGPSVFPPLAPCSRSTSESTA LGCLVKDYFPEPVTVSWNSGALTSQVHTFPAVLQSSGLYSLSSVTVTPSSSLGKTKYTCNV VDKRVESKYGPPCPPEPEFLGGPSVFLFPPKPKDTLMI SRTP EVT CVVVDVSDQEDPEVQFNWYVDG EVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQP REPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTV DKSRWQEGNVFSCVMHEALHNHYTQKSLSLSLG |
| 447 | G12-hLambda LC | QSVLTQPPASGTPGQRVTISCSGNTSNI GRESVYVYQQLPGTAPKLLIY LNSQRPSGVPDRESGSKSG TSASLAI SGLQSEDEADYYCGTWDDSLNGWVFGGGTKLTVLGQPKAAPSVTLLEPPSSEELQANKATLVC LISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNKYAASSYLSLTPEQWKS HRYSYSCQVTHEGSTVE KTVAPTECS |
| 448 | pCMV6-hygro-HA-cyno-PD-1 (1-185) | aacaaaaatattaacgcttacaatttccattcgccattcaggctgcgcaactgttggaaggggcgaatcgg tcggggcctcttcgctattacgcccagctggcgaaagggggatgtgctgcaaggcgaataggtgggtaa cgccagggttttcccagtcacgacgttgtaaaacgacggccagtgccaagctgatctacatggaatc aatatggcaattagccatattagtcattggttatatagcataaatcaatattggctattggccattgc atcgttgatctatatacaaatatgtacattatattggctcatgtccaatagaccgccatctatgac attgattatgactagttatataatagtaatacaattacggggcattagtcattagccatataatggatt |

TABLE 29-continued

| Sequences | |
|-----------------|---|
| SEQ ID NO: Name | Sequence |
| | tccgcgttacataaacttacggtaaatggcccgctggctgacgcgccaacgaccccgcccatgacgt caataatgacgtatgtccccatagtaacgccaatagggacttccattgacgtcaatgggtggagtatt tacggtaaaactgccacttggcagtaacatcaagtgtatcatatgccaagtccgccccctatgacgtca atgacggtaaatggcccgctggcatatgcccagtaacatgacctacgggacttccctacttggcagt acatctacgtattagtcacgctattaccatggatgacgggttttggcagtaaccaaatggcgtggat agcggttgactcacgggatttccaagtccacccccatgacgtcaatgggagtttgttttggcacc aaaaacaacgggacttccaaaatgtcgttaaaccccccgctgacgcaaatggcggtaggcgtg tacggtagggagggtctataaagcagagctcgtttagtgaaccgtcagaatttgttaaacgactca tagggcggcgggaatcgtcgactggatccggtaaccgaggagatctgcccgcgcatcgccggcggc cagatctcaagcttatggacatgcccgtgcccagcaaaccttctcggtactactattgttatggctcgag gtgcgctggtatccttacgacgtgcctgactacgccccaggatgggtccttagagtcaccagacagg cctggaaacccccacttctccccagcctgctcctggtgaccgaaggggacaacgcccacttcaact gcagcttctccaacgcatcgagagcttctgctaaactggtagagatgagccccagcaaacagacgg caagctggccgcttccccagggaccgacgcccagcccgccaggactgcccgttccgtgtcacagcc tgcccaacggcgtgacttccacatgagcgtggtagggccccggcgaatgacagcggcactacctct gtggggccatctcctggcccccaaggcagatcaaaagagagctgcccggcagagctcagggtgacag agagaagggcagaagtccccacagccccacccccctcaccagggcagcggccagtccaagccc tgggtggttgggtgctggtggcagcctggtgctgctagtctgggtcctggcctgcatct gtcccgcgcccacaaaggacaatagaagcaggcgcacctgacgcttaagcggcggcactcgaggt ttaaaccggccggcggcctcatagctggttccctgaacagatccccgggtggcatccctgtgacccc cagtgctctcctggccctggaagtggcactccagtgcccacagccttgtcctaataaaaaataagt gcatcatttgtctgactaggtgctcctctataatataatggggtggaggggggtggtatggagcaag ggcaagtgggaagacaacctgtagggcctcgggggtctattgggaaccaagctggagtgacgtggcac aatctggctcactgcaatctccgctcctgggtcaagcagatctcctgctcagcctcccaggtgt tgggttccagcagatgcatgaccaggctcagctaattttgttttttggtagagacggggtttcca tatggccaggctggtctccaactcctaactcaggtgatctaccaccttggcctcccaaatctctgg gat tacaggcgtgaaccactgctccttccctgctctctgattttaaataactataccagcaggagg acgtccagacacagcataggctacctggccatgcccacacggtagggacatttgagttgcttcttggca ctgctctctcatgcttgggtccactcagtagatgcttgaatttggtagcggcggcagcttccgtagt ggatgtgtgctcagttagggtgtggaaagtccccaggctcccagcagcagaagtagcgaagcagc atctcaattagtcagcaaccaggtgtgaaagtccccaggctcccagcagcagaagtagcgaagca tgcatctcaattagtcagcaaccaggtgtgaaagtccccaggctcccagcagcagaagtagcgaagca gttccgcccattctccgccccatggctgactaattttttttatattagcagagggcagagggcggcctcgg cctctgagctattccagaagtgtgaggaggcttttttggggcctaggcttttgcataaaagctccccgg gagcttgtatccatttccggtctgtagcagagacagctacgaccatgaaaaagcctgaaactccagc cgactctgttgagaagtctctgatcgaaaagtgcacagcgtctccgacctgatgcagctctcggagg gcaagaatctcgtgcttccagctcagatgtagggggcgtggatagctcctcggggtaaatagctgccc cgatgggttctacaagatcgttatggttatcggcacttggcatcggccgctcctccgatccggaag tgcttgacattggggaatttagcagagagctgacctattgcatctcccgcgtgacacaggggtgacag tgcaagacctgctgaaacccaacttggccgctgtctcgaacacggctcggcggggccatggatgcaatcg tgcggccgactctagccagacgagcgggttgggcccattcggacccgcaaggaatcgggtcaatcactca catggcgtgatctcatatgcccagatgctgatccccatggtatcactggcaaacctgtagggagaca ccgctcagtgctcgtcggcagagctctcagtagctgatgcttgggcccaggactgcccgaagctcc ggcactcgtgcaacgggttccggctcccaaatgctcctgacggacaatggccgcatatacagcggctca ttgactggagcagggcgtgctcggggatccccaatcagaggctcgcacaacatctctctggaggccgt ggttggcttgtatggagcagcagacgctactctgagcggaggcatcgggagcttgcaggatcgccgc ggctcgggctgataatgctccgcttggctctgaccaactctatcagagcttgggtgacggcgaattcgc atgatgcagcttgggcccagggctcagtcgacgcaatcgtccgatccggagccgggactgctcgggctga cacaatcggccgcaagcggcggcctctggaccagatggctggtagaagtactcggcagatagtgaa accgacccccagcactcgtccgagggcaaaaggaatagctgacagcgggactctgggggtcgaatgacc gaccaagcagcggcccaactcggcactcagagatctcagatccaccgcccctctatgaaaggttgggc tccggaatcgtttccgggacgcccggctggatgactcctcagcggcgggatactcatgctggagttcttc gccccccaactggtttatgacagcttataatggttacaataaaagcaatagcatcacaatctcaca aataaagcattttttcactgcatctagttgtggtttgtccaaactcactcaatgtatcttcatctgct tgtataccgtcgacctctagctagagcttggcgtaatcatggtcatagctgttctcctgtgtaaatgt tatccgtcacaattccacacaacatcagagccggaaagcataaagtgtaaagcctggggtgctcaatga gtgagctaaactacat taatgctgtgctgctcactgcccgttccagtcgggaaacctgctgctgcccag ctgcattaatgaatcggccaacgcgcggggagaggcgttggcgtattgggctcttccgctctcctcgt ctcactgactcgtcgcgctcgtcgtcgtcggctgcccagcgggtatcagctcactcaaaaggcgttaata cgggttatccacagaatcaggggat aacgcaggaagaacatgtgagcaaaaggccagcaaaaggccagg aacctgaaaaaggccgcttggcggcttttccataggctcccggccccctgacgagcatcacaaaaat cagcgtcaagtacaggggtggcgaaccccgacaggaactataaagat accagcgttccccctggaaagc tccccctgctgctctcctgttccgaccctgcccgttaccggatacctgtcggccttctccctcgggga agcgtggcgttctcctatagctcacgctgtaggtatctcagtcgggtgtaggtcgtctcgtccaagctg ggctgtgtgacgaacccccgctcagcccagcggctgccccttaccggtaactatcgtcttggatcc aacccggtaagcacgacttatcggcactggcagcagccactggtaacaggatagcagagcggaggtat gtaggcgggtgctacagagttcttgaagtggtggcctaactacggctacactagaagaacagttttggt atctcggctcgtcgaagccagttaccctcggaaaaagagttggtagctcttggatcggcgaacacaac accgctggtagcgggtggttttttggtttgaacagcagcagattacgcgcagaaaaaaggatctcaagaa gatcctttgatctttctacggggtctgacgctcagtggaacgaaaaactcaggttaagggttttggct atgagatatacaaaaggatctcaccctagatccttttaaat taaaaatgaagttttaaatacaata agttatataatgagtaaaacttggctcagcagttaccaatgcttaatacagtgaggcaactctcagcgtc tgtctattctgctcactcagttgctgactccccctgctgtagataaactacgatacgggagggctta coatcggccccagtgctgcaatgat acccgagacccacgctcaccggctccagatttatcagcaata aaccagccagccggaagggccgagcagaggtggtcctgcaactttatccgctccatccagctctatt |

TABLE 29-continued

| Sequences | | |
|---|---|--|
| SEQ ID NO: Name | Sequence | |
| | aattgttgccgggaagctagagtaagtagttcgccagttaatagtttgcgcaacggtgttgccattgct acaggcatcgtggtgtcaagctcgtcgtttggtatggcttcattcagctccggttcccacgatcaagg cgagtacatgatccccatgtgtgcaaaaaagcggtagctcctcggctcctccgatcgttgtcaga agt aagt tggccgcagtggtatcactcatgggtatggcagcactgcataattctcttactgtcatgcca tccgt aagatgctttctgtgactggtgagtagctcaaccaagtcattctgagaatagtgtagcggcga ccgagtgctcttgcccggcgtcaatcgggataaataccgcccacatagcagaactttaaagtgtc atcattggaaaaagctctcggggcgaaaaactcacaaggatcttaccgctgttgagatccagttcgatg taaccactcgtgcaccacaactgactctcagcatctttactttaccagcgtttctgggtgagcaaaa acaggaaggcaaatgccgcaaaaaagggat aagggcgacacggaaatggtgaatactcactcttct ctctttcaatattattgaagcattatcagggttattgtctcatgagcggat acatattgaatgtatt tagaaaaat aaacaaatagggttccgcgcacatttcccgaagaagtgccacctgacgcgacctgagc ggccat taagcggcgggggtgtggtggttacgcgcagcgtgaccgctacacttgcacgcccctagcg cccgctcctttcgcttcttccctctcttctcgcacgcttgcggcttcccccgtcaagctcctaaat cggggctcctttaggggtccgatttagtgctttacggcactcgcaccccaaaaacttgatagggt gatggttcaogtagtgggcatcgccctgatagacggttttgcctcttgacgtggagtcacagctt tttaatagtgagctctgttccaaactggaaacaactcaacctatctcgtctattcttttgattta taagggtttgcccatttccgctattgggttaaaaaatgagctgatttaacaaaaatttaacgcgaat ttt | |
| 449 Abz1mod-hIgG4 HC | QVQLVQSGSELKPKGASVKVSKASGYTFTSYAMHWVRQAPGGLEWMGYISPFTRATYAQGFTRGV FSLDTSVSTAYLQISSLKAEDTAVYYCARDYDYYRYAMDYWGQGTIVTVSSASTKGPSVFLPAPCSR TSESTAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNV HKPSNTKVDKRVESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQ FNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKQPR EPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVD KSRWQEGNVFSCSVMHLEHNNHYTQKLSLSL | |
| 450 Abz1mod-hKappa LC | EIVLTQSPDFQSVTPKEKVTITCRASQSI PPQFLHWYQQKPDQSPKLLI KAASQRASGVPSRESGSGG DFTLTINSLEAEDAATYYCHQFHSPLTFGGGKLEIKRTVAAPSVFIFPPSDEQLKSGTASVCLLN NFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSSTYLSLSTLTLSKADYEKHKVYACEVTHQGLSPVT KSENRGEC | |
| 451 Anti-hPD-1 #1- hIgG4-L6-hIL-2 (D20A/R38E) HC Linker in dashed underline hIL-2 in italics | QVQLVESGGGVVQPGRSLRLDCKASGITFSNSGMHWVRQAPGKLEWVAVIWDGSKRYADSVKGR ETSRDNSKNTLFLQMNSLRAEDTAVYYCATNDYWGQGLVTVSSASTKGPSVEPLAPCSRSTSESTA ALCGLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNV DHKPSNTKVDKRVESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQ FNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKQPR EPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVD KSRWQEGNVFSCSVMHLEHNNHYTQKLSLSLGLKSGGGGSAPTSSSTTKKTQLQLEHLLALQMI LINGIN <i>EMLTFKFYMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLELKGSETTEMCE YADETATIVEFLNRWITFCQSIISTLT</i> | |
| 452 Anti-hPD-1 #1- hKappa LC | EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLIYDASNRAITGIPARESGSGG DFTLTISLSEPEDFAVYYCQQSSNWPRTPFGGQTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVCLLN NFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSSTYLSLSTLTLSKADYEKHKVYACEVTHQGLSPVT KSENRGEC | |
| 453 OMC.1.B6- hIgG4-L6-hIL-2 (D20A/R38E) HC Linker in dashed underline hIL-2 in italics | EVQLLESGGGLVQPGGSLRLSCAASGFTESNYSWVRQAPGKLEWVSAISSGGTIFYADSVKGR ETSRDNSKNTLYLQMNSLRAEDTAVYYCAKHKWNAVYDGMVDVWGQGTIVTVSSASTKGPSVFLPAPCSR STSESTAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNV DHKPSNTKVDKRVESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQ FNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKQPR EPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVD KSRWQEGNVFSCSVMHLEHNNHYTQKLSLSLGLKSGGGGSAPTSSSTTKKTQLQLEHLLALQMI LINGINNYKPKL <i>NNYKPKLTEM LTFKFYMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLELKG SETTEMCEYADETATIVEFLNRWITFCQSIISTLT</i> | |
| 454 OMC.2.C6- hIgG4-L6-hIL-2 (D20A/R38E) HC Linker in dashed underline hIL-2 in italics | EVQLLESGGGLVQPGGSLRLSCTASGFTFSSYEMQWVRQAPGKLEWVLGITSSSSHIFYADSVKGR ETSRDNSKNTLYLQMNSLRAEDTAVYYCTKDLNSYGLDVGQGTIVTVSSASTKGPSVEPLAPCSRST ESTAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNV DHKPSNTKVDKRVESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQ FNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKQPR EPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVD KSRWQEGNVFSCSVMHLEHNNHYTQKLSLSLGLKSGGGGSAPTSSSTTKKTQLQLEHLLALQMI LINGINNY <i>KNPKLTEM LTFKFYMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLELKGSE TTFMCEYADETATIVEFLNRWITFCQSIISTLT</i> | |
| 455 OMC.1.D6- hIgG4-L6-hIL-2 (D20A/R38E) HC Linker in dashed | EVQLLESGGGLVQPGGSLRLSCAASGFTFSDYYMSWVRQAPGKLEWVSAISSGGTIFYADSVKGRFI ISRDNSKNTLYLQMNSLRAEDTAVYYCAKHKWNAVYDGMVDVWGQGTIVTVSSASTKGPSVFLPAPCSR STSESTAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNV DHKPSNTKVDKRVESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQ FNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKQPR | |

TABLE 29-continued

| Sequences | | |
|------------|--|--|
| SEQ ID NO: | Name | Sequence |
| | underline | REPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTV |
| | hIL-2 in | RWQEGNVFSCSVMHEALHNHYTQKLSLSLGKSGGGGSAPTSSTTKKTQLQLEHLLALQMI LNGINNY |
| | italics | <i>NNYKNPKLTEMLETFKFYMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLELKGSETTEMCEYADETATIVEFLNRWITFCQSIISTLT</i> |
| 456 | D12-hIgG4-df-hIL-2 (D20A/R38E) HC hIL-2 in italics | DVQLVESGGGLVQPGGSLRLSCAASGFTFDISAMSWVRQAPGKGLEWVSTISGSAYSTYYADSVKGRFTISRDNKSTLYLQMNLSRAEDTAVYYCAREIFSDYWGGLGLTVTVSSASTKGPSVFPPLAPCSRSTSESTALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPPSSSLGKTKYTCNVDPKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKLSLSLGKAPTSSSTTKKTQLQLEHLLALQMI LNGINNYKNPKLTEMLETFKFYMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLELKGSETTEMCEYADETATIVEFLNRWITFCQSIISTLT |
| 457 | G12-hIgG4-df-hIL-2 (D20A/R38E) HC hIL-2 in italics | DSLVESGGGLVQPGGSLRLSCAASGFTFDISAMSWVRQAPGKGLEWVSTISGSAYSTYYADSVKGRFTISRDNKSTLYLQMNLSRAEDTAVYYCAREIFSDYWGGLGLTVTVSSASTKGPSVFPPLAPCSRSTSESTALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPPSSSLGKTKYTCNVDPKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKLSLSLGKAPTSSSTTKKTQLQLEHLLALQMI LNGINNYKNPKLTEMLETFKFYMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLELKGSETTEMCEYADETATIVEFLNRWITFCQSIISTLT |
| 458 | 2H7-hIgG4-LE HC | EVQLLESGGGLVQPGGSLRLSCAASGFTFKDYCMTWVRQAPGKGLEWVSAIVYSGGSTYYADSVKGRFTISRDNKNTLYLQMNLSRAEDTAVYYCAKYTRASYFYDAMDVWGQTTVTVSSASTKGPSVFPPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPPSSSLGKTKYTCNVDPKPSNTKVDKRVESKYGPPCPPCPAPEFEGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKLSLSLG |
| 459 | 2H7-hIgG4-LAGA HC | EVQLLESGGGLVQPGGSLRLSCAASGFTFKDYCMTWVRQAPGKGLEWVSAIVYSGGSTYYADSVKGRFTISRDNKNTLYLQMNLSRAEDTAVYYCAKYTRASYFYDAMDVWGQTTVTVSSASTKGPSVFPPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPPSSSLGKTKYTCNVDPKPSNTKVDKRVESKYGPPCPPCPAPEFAGAPSVELFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKLSLSLG |
| 460 | OMC.2-A3-hIgG4/A HC | EVQLLESGGCLVQPGGSLRLSCAASGFTESDYMSWVRQAPGKGLEWVSAISSGGTIFYADSVKGRFTISRDNKNTLYLQMNLSRAEDTAVYYCAKHKWVNDVYDAMDVWGQTTVTVSSASTKGPSVFPPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPPSSSLGKTKYTCNVDPKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKLSLSLG |
| 461 | OMC476pH7-hIgG4 HC | DMQLVESGGGVVRPGESLRLSCTASGFTFSISAMSWVRQAPGKGLEWVSAISGTAYSTYYADSVRGRETISRDNKNTLYLQMNLSRAEDTAVYYCAKDNFFDYWGLGLTVTVSSASTKGPSVFPPLAPCSRSTSESTALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPPSSSLGKTKYTCNVDPKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKLSLSLG |
| 462 | OMC476pB11.H7 LC | QSVMTQPPSASGTPGQRVTTISCSGVTSNIGSNVYVYQQLPGTAPKLLIYLNLSQRPSGVPDRESGSKSGTSASLAI SGLQSEDEADYCYGTVWDDSLNGWVFGGGTKLTVLQGPKAAPSVTLFPPSSSEELQANKATLVCLISDEYPGA VTVAVKADSSPVKAGVETTTPSKQSNKYAASSYLSLTPBQWKSHRSYSCQVTHEGSTVEKTVAPTECS |
| 463 | OMC476pB11-hIgG4 HC | DVQLVESGGGVVRPGESLRLSCTASGFTFSISAMSWVRQAPGKGLEWVSAISGTAYSTYYADSVRGRETISRDNKNTLYLQMNLSRAEDTAVYYCAKDNFFDYWGLGLTVTVSSASTKGPSVFPPLAPCSRSTSESTALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPPSSSLGKTKYTCNVDPKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKLSLSLG |
| 464 | OMC476pG10-hIgG4 HC | DVQLVESGGGVVRPGGSLRLSCAASGFTFSIYAMSWVRQAPGEGLEWVSHISASGGSTYYADSVKGRFTAISRDNKNTLYLQMNLSRAEDTAVYYCTTNLGSYWGGLGLTVTVSSASTKGPSVFPPLAPCSRSTSESTALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPPSSSLGKTKYTCNVDPKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWYVDG |

TABLE 29-continued

| Sequences | | |
|-----------|--|---|
| SEQ ID | Name | Sequence |
| | | VEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSRLTVDKSRWQEGNVFSCVMHEALHNHYTQKLSLSLGLG |
| 465 | OMC476pH10-hIgG4 HC | DVQLVESGGGVVPRGGSRLRSCAASGFTFSIYAVSWVRQAPGEGLEWVSHISASGGSTYYADSVKGRFAISRDN SKNTLYLQMNSLRAEDTAVYYCTTNLGS DYWGLGTLVTVSSASTKGPSVFP LAPCSRSTSESTAAALGCLVKDYFPEPVTVSWNSGALTS GVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVN HKPSNTKVDKRVESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSRLTVDKSRWQEGNVFSCVMHEALHNHYTQKLSLSLGLG |
| 466 | OMC476pG10.H10 LC | QSVLTQPPASGTPGQRVTISCSGYSYSDIGTNYVYVYQQLPGTAPKLLIFATDRRPSGVPDRESGSKGTSASLAI SGLQSEDEADYYCGTWDDSLN VVWVFGGGTKLTVLGQPKAAPSVTLLEPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNKYAASSYLSLTP EQWKS HRYSYSCQVTHEGSTVEKTVAPTECS |
| 467 | OMC476pE4-hIgG4 HC | DVQLVESGGGVVPRGGSRLRSCAASGFTFSTDAMGWVRQAPGEGLEWVSLISGGSTYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAKNSLAFPDYWGGLTVTVSSASTKGPSVFP LAPCSRSTSESTAAALGCLVKDYFPEPVTVSWNSGALTS GVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVN HKPSNTKVDKRVESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSRLTVDKSRWQEGNVFSCVMHEALHNHYTQKLSLSLGLG |
| 468 | OMC476pE4 LC | QSVLTQPPASGTPGQRVTISCSGGSNIGRESVNWYQQLPGTAPKLLIYSTDRRPSGVPDRESGSKGTSASLAI SGLQSEDEADYYCGTWDDSLN VVWVFGGGTKLTVLGQPKAAPSVTLLEPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNKYAASSYLSLTP EQWKS HRYSYSCQVTHEGSTVEKTVAPTECS |
| 469 | J110-hIgG1 HC | DVQLQESGPGLVKPSQSLSLTCTVTGHSITSDYAWNWIQFP GDKLEWMMGYISYSGYTTYNPSLKS RVSI TRDTSKNQFFLQLNSVTTEDTATYPCARDLDYGPWFAYWGQGLTVTVSAASTKGPSVFP LAPSSKSTSGTAAALGCLVKDYFPEPVTVSWNSGALTS GVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVN HKPSNTKVDKRVESKYGPPCPPAPELGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSKLTVDKSRWQEGNVFSCVMHEALHNHYTQKLSLSLSPGK |
| 470 | J110-hKappa LC | DIQMTQSPASLSASVGETVTLTCSRASENIHNYLAWYQQKQKSPQLLVYNVKTADGVPSRFGSGSGGTQYSLKINS LQPEDFGSYQCQHPWSSPWTFGGGTKVEIKRTVAAPSVFI FPPSDEQLKSGTASVVCLLNNFYPRKAVQWKVDNALQSGNSQESVTEQDSKDSYSLSSLTLSKADY EKHKVYACEVTHQGLSSPVTKSENRRGEC |
| 471 | 2H7-hIgG1-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) HC hIL2 in italics | EVQLLESGGGLVQPGGSLRSLRSCAASGFTFKDYCMTWVRQAPGKLEWVSAIVYSGGSTYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAKYTRASYFYDAMDVWGQGT TTVTVSSASTKGPSVFP LAPSSKSTSGTAAALGCLVKDYFPEPVTVSWNSGALTS GVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVN HKPSNTKVDKRVESKYGPPCPPAPELAGAPSVLFPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSKLTVDKSRWQEGNVFSCVMHEALHNHYTQKLSLSLPGKAPASSSTKKTQLQLEHLLALQMI LINGINNYKNP KLTLEMLTFK FYPMPK KATELKHLCLEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLELKGSETTE |
| 472 | 2H7-hIgG4-LE-df-hIL-2 (T3A/D20A/R38E/C125A) HC hIL-2 in italics | EVQLLESGGGLVQPGGSLRSLRSCAASGFTFKDYCMTWVRQAPGKLEWVSAIVYSGGSTYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAKYTRASYFYDAMDVWGQGT TTVTVSSASTKGPSVFP LAPCSRSTSESTAAALGCLVKDYFPEPVTVSWNSGALTS GVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVN HKPSNTKVDKRVESKYGPPCPPAPEFEGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSRLTVDKSRWQEGNVFSCVMHEALHNHYTQKLSLSLPGKAPASSSTKKTQLQLEHLLALQMI LINGINNYKNP KLTLEMLTFK FYPMPK KATELKHLCLEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLELKGSETTE |
| 473 | 2H7-hIgG1-LAGA--df-hIL-2 (T3A/D20A/R38E/C125A) HC hIL-2 in italics | EVQLLESGGGLVQPGGSLRSLRSCAASGFTFKDYCMTWVRQAPGKLEWVSAIVYSGGSTYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAKYTRASYFYDAMDVWGQGT TTVTVSSASTKGPSVFP LAPCSRSTSESTAAALGCLVKDYFPEPVTVSWNSGALTS GVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVN HKPSNTKVDKRVESKYGPPCPPAPEFAGAPSVLFPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSRLTVDKSRWQEGNVFSCVMHEALHNHYTQKLSLSLPGKAPASSSTKKTQLQLEHLLALQMI LINGINNYKNP KLTLEMLTFK FYPMPK KATELKHLCLEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLELKGSETTE |

TABLE 29-continued

| Sequences | | |
|------------|---|--|
| SEQ ID NO: | Name | Sequence |
| 474 | 2H7-hIgG1-LAGA-df-hIL-2 (T3A/R38E/I92K/C125A) HC hIL-2 in italics | EVQLLESGGGLVQPGGSLRLSCAASGFTFKDYCMTWVRQAPGKGLEWVSAIVYSGGSTYYADSVKGRFT ISRDNKNTLYLQMNLRADTAVYYCAKYTRASYFYDAMDVWGQTTVTVSSASTKGPSVFPPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSVHTFPFPAVLQSSGLYSLSVVTVPSSSLGTQTYICNV NPKPSNTKVDKRVESKYGPPCPPCPAPEFAGAPSVELFPPKPKDTLMI SRTPPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI SKAK GQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSK LTVDKSRWQGNVFCSCVMHEALHNHYTQKSLSLSPGKAPASSSTKKTQLQLEHLLLDLQMLNNGINNY KNPKLTEMLELTKFKFYPMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLI SNINVKVLELKGSE TTFMCEYADETATIV EFLNRWITFAQSII STLT |
| 475 | 2H7-hIgG4-LE-df-hIL-2 (T3A/R38E/192K/C125A) HC hIL-2 in italics | EVQLLESGGGLVQPGGSLRLSCAASGFTFKDYCMTWVRQAPGKGLEWVSAIVYSGGSTYYADSVKGRFT ISRDNKNTLYLQMNLRADTAVYYCAKYTRASYFYDAMDVWGQTTVTVSSASTKGPSVFPPLAPCSR STSESTAALGCLVKDYFPEPVTVSWNSGALTSVHTFPFPAVLQSSGLYSLSVVTVPSSSLGTQTYICNV DHKPSNTKVDKRVESKYGPPCPPCPAPEFAGAPSVELFPPKPKDTLMI SRTPPEVTCVVVDVSHEDP FNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQP REPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTV DKSRWQGNVFCSCVMHEALHNHYTQKSLSLSPGKAPASSSTKKTQLQLEHLLLDLQMLNNGINNYKNP KLEMLELTKFKFYPMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLI SNINVKVLELKGSE TTFMCEYADETATIV EFLNRWITFAQSII STLT |
| 476 | 2H7-hIgG4-LAGA-df-hIL-2 (T3A/R38E/192K/C125A) HC hIL-2 in italics | EVQLLESGGGLVQPGGSLRLSCAASGFTFKDYCMTWVRQAPGKGLEWVSAIVYSGGSTYYADSVKGRFT ISRDNKNTLYLQMNLRADTAVYYCAKYTRASYFYDAMDVWGQTTVTVSSASTKGPSVFPPLAPCSR STSESTAALGCLVKDYFPEPVTVSWNSGALTSVHTFPFPAVLQSSGLYSLSVVTVPSSSLGTQTYICNV DHKPSNTKVDKRVESKYGPPCPPCPAPEFAGAPSVELFPPKPKDTLMI SRTPPEVTCVVVDVSHEDP FNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQP REPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTV DKSRWQGNVFCSCVMHEALHNHYTQKSLSLSPGKAPASSSTKKTQLQLEHLLLDLQMLNNGINNYKNP KLEMLELTKFKFYPMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLI SNINVKVLELKGSE TTFMCEYADETATIV EFLNRWITFAQSII STLT |
| 477 | 2H7-hIgG1-LAGA-df-hIL-2 (T3A/R38E/D84K/C125A) HC hIL-2 in italics | EVQLLESGGGLVQPGGSLRLSCAASGFTFKDYCMTWVRQAPGKGLEWVSAIVYSGGSTYYADSVKGRFT ISRDNKNTLYLQMNLRADTAVYYCAKYTRASYFYDAMDVWGQTTVTVSSASTKGPSVFPPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSVHTFPFPAVLQSSGLYSLSVVTVPSSSLGTQTYICNV NPKPSNTKVDKRVESKYGPPCPPCPAPEFAGAPSVELFPPKPKDTLMI SRTPPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI SKAK GQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSK LTVDKSRWQGNVFCSCVMHEALHNHYTQKSLSLSPGKAPASSSTKKTQLQLEHLLLDLQMLNNGINNY KNPKLTEMLELTKFKFYPMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLI SNINVI VLELKGSE TTFMCEYADETATIV EFLNRWITFAQSII STLT |
| 478 | 2H7-hIgG4-LE-df-hIL-2 (T3A/R38E/D84K/C125A) HC hIL-2 in italics | EVQLLESGGGLVQPGGSLRLSCAASGFTFKDYCMTWVRQAPGKGLEWVSAIVYSGGSTYYADSVKGRFT ISRDNKNTLYLQMNLRADTAVYYCAKYTRASYFYDAMDVWGQTTVTVSSASTKGPSVFPPLAPCSR STSESTAALGCLVKDYFPEPVTVSWNSGALTSVHTFPFPAVLQSSGLYSLSVVTVPSSSLGTQTYICNV DHKPSNTKVDKRVESKYGPPCPPCPAPEFAGAPSVELFPPKPKDTLMI SRTPPEVTCVVVDVSHEDP FNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQP REPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTV DKSRWQGNVFCSCVMHEALHNHYTQKSLSLSPGKAPASSSTKKTQLQLEHLLLDLQMLNNGINNYKNP KLEMLELTKFKFYPMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLI SNINVI VLELKGSE TTFMCEYADETATIV EFLNRWITFAQSII STLT |
| 479 | 2H7-hIgG4-LAGA-df-hIL-2 (T3A/R38E/D84K/C125A) HC hIL-2 in italics | EVQLLESGGGLVQPGGSLRLSCAASGFTFKDYCMTWVRQAPGKGLEWVSAIVYSGGSTYYADSVKGRFT ISRDNKNTLYLQMNLRADTAVYYCAKYTRASYFYDAMDVWGQTTVTVSSASTKGPSVFPPLAPCSR STSESTAALGCLVKDYFPEPVTVSWNSGALTSVHTFPFPAVLQSSGLYSLSVVTVPSSSLGTQTYICNV DHKPSNTKVDKRVESKYGPPCPPCPAPEFAGAPSVELFPPKPKDTLMI SRTPPEVTCVVVDVSHEDP FNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQP REPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTV DKSRWQGNVFCSCVMHEALHNHYTQKSLSLSPGKAPASSSTKKTQLQLEHLLLDLQMLNNGINNYKNP KLEMLELTKFKFYPMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLI SNINVI VLELKGSE TTFMCEYADETATIV EFLNRWITFAQSII STLT |
| 480 | 1H3-hIgG4-df-hIL-2 (WT) HC hIL-2 in italics | EVQLVESGGGLVQPGRLSLKLSCAVSGFTFSDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGRFT ISRDNKNTLYLQMNLRSEDATAYCARHSGSYFDYWGQGMVTVSSASTKGPSVFPPLAPCSRSTSES TAALGCLVKDYFPEPVTVSWNSGALTSVHTFPFPAVLQSSGLYSLSVVTVPSSSLGTQTYICNV NPKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQP REPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTV DKSRWQGNVFCSCVMHEALHNHYTQKSLSLSPGKAPASSSTKKTQLQLEHLLLDLQMLNNGINNYKNP KLEMLELTKFKFYPMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLI SNINVI VLELKGSE TTFMCEYADETATIV EFLNRWITFAQSII STLT |
| 481 | 1H3-hIgG4-L6-hIL-2 (WT) HC Linker in dashed | EVQLVESGGGLVQPGRLSLKLSCAVSGFTFSDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGRFT ISRDNKNTLYLQMNLRSEDATAYCARHSGSYFDYWGQGMVTVSSASTKGPSVFPPLAPCSRSTSES TAALGCLVKDYFPEPVTVSWNSGALTSVHTFPFPAVLQSSGLYSLSVVTVPSSSLGTQTYICNV NPKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQP REPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTV DKSRWQGNVFCSCVMHEALHNHYTQKSLSLSPGKAPASSSTKKTQLQLEHLLLDLQMLNNGINNYKNP KLEMLELTKFKFYPMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLI SNINVI VLELKGSE TTFMCEYADETATIV EFLNRWITFAQSII STLT |

TABLE 29-continued

| Sequences | | |
|-----------|--|--|
| SEQ ID | Name | Sequence |
| | underline hIL-2 in italics | DGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDNLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQV YTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRW QEGNVFSCSVMHEALHNHYTQKLSLSLGLKSGGGGSAPTSSSTKKTQLQLEHLLLDLQMLINGINNYKN PKLTRMLTFKPYMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLELKGSETT FMCEYADETAT IVEFLNRWITFCQSI IISTLT |
| 482 | 1H3-hIgG4 HC | EVQLVESGGGLVQPGRSLKLSCAVSGFTESDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGRFT ISRDNAKITLYLQMDSLRSEDATATYYCARHSGGYFDYWGQGMVTVSSASTKGPSVFPPLAPCSRSTSES TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNVNHHKPS NTKVDKRVESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQENWYV DGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDNLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQV YTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRW QEGNVFSCSVMHEALHNHYTQKLSLSLGL |
| 483 | 1H3-hKappa-df- hIL-2 (WT) LC hIL-2 in italics | DTVLTQSPALAVSPGERVTISCRASESVRTGVHWYQQKPGQPKLLIYGASNLESVGPAPRFSGSGSGTD FTLTIDPVEADDTATYFCQQSWNDPPTFGSGTKLEIKRTVAAPSVPFIPPPSDEQLKSGTASVVCLLMNE YPREAKVQWKVDNALQSGNSQESVTEQDSKSTYSLSSITLTKADYEKHKVYACEVTHQGLSPVTKS FNRGECAPTSSTKKTQLQLEHLLLDLQMLINGINNYKNPKLTRMLTEKFYMPKKA TELKHLQCLEEEL KPLEEVLNLAQSKNFHLRPRDLISNINVI VLELKGSETTEMCEYADETAT IVEFLNRWITFCQSI IISTLT T |
| 484 | 1H3-hKappa-L6- hIL-2 (WT) LC Linker in dashed underline hIL-2 in italics | DTVLTQSPALAVSPGERVTISCRASESVRTGVHWYQQKPGQPKLLIYGASNLESVGPAPRFSGSGSGTD FTLTIDPVEADDTATYFCQQSWNDPPTFGSGTKLEIKRTVAAPSVPFIPPPSDEQLKSGTASVVCLLMNE YPREAKVQWKVDNALQSGNSQESVTEQDSKSTYSLSSITLTKADYEKHKVYACEVTHQGLSPVTKS FNRGECSGGGGSAPTSSSTKKTQLQLEHLLLDLQMLINGINNYKNPKLTRMLTFKPYMPKKA TELKHLQ CLEEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLELKGSETTEMCEYADETAT IVEFLNRWITFCQ SI IISTLT |
| 485 | 1H3-hIgG4-L6- hIL-2 (D20Y) HC Linker in dashed underline hIL-2 in italics | EVQLVESGGGLVQPGRSLKLSCAVSGFTFSDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGRFT ISRDNAKITLYLQMDSLRSEDATATYYCARHSGGYFDYWGQGMVTVSSASTKGPSVFPPLAPCSRSTSES TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNVNHHKPS NTKVDKRVESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYV DGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDNLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQV YTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRW QEGNVFSCSVMHEALHNHYTQKLSLSLGLKSGGGGSAPTSSSTKKTQLQLEHLLLDLQMLINGINNYKN PKLTRMLTFKPYMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLELKGSETT FMCEYADETAT IVEFLNRWITFCQSI IISTLT |
| 486 | 1H3-hIgG4-df- hIL-2 (D20Y) HC hIL-2 in italics | EVQLVESGGGLVQPGRSLKLSCAVSGFTFSDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGRFT ISRDNAKITLYLQMDSLRSEDATATYYCARHSGGYFDYWGQGMVTVSSASTKGPSVFPPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHHKPS NTKVDKRVESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKEN WYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDNLNGKEYKCKVSNKALPAPIEKTI SKAKGQPRE PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRW QEGNVFSCSVMHEALHNHYTQKLSLSLGLKAPTSSSTKKTQLQLEHLLLYLQMLINGINNYKNPKLTRM LTFKPYMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLELKGSETTEMCEYA DETAT IVEFLNRWITFCQSI IISTLT |
| 487 | 1H3-hIgG1-df- hIL-2 (D20Y) HC hIL-2 in italics | EVQLVESGGGLVQPGRSLKLSCAVSGFTFSDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGRFT ISRDNAKITLYLQMDSLRSEDATATYYCARHSGGYFDYWGQGMVTVSSASTKGPSVFPPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHHKPS NTKVDKRVESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKEN WYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDNLNGKEYKCKVSNKALPAPIEKTI SKAKGQPRE PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRW SRWQQNVFSCSVMHEALHNHYTQKLSLSLSPGKAPTSSSTKKTQLQLEHLLLYLQMLINGINNYKNPKL TRMLTFKPYMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLELKGSETTEMCE EYADETAT IVEFLNRWITFCQSI IISTLT |
| 488 | 1H3-hIgG4-L6- (D20A/R38P) HC Linker in dashed underline hIL-2 in italics | EVQLVESGGGLVQPGRSLKLSCAVSGFTFSDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGRFT ISRDNAKITLYLQMDSLRSEDATATYYCARHSGGYFDYWGQGMVTVSSASTKGPSVFPPLAPCSRSTSES TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNVNHHKPS NTKVDKRVESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQENWYV DGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDNLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQV YTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRW QEGNVFSCSVMHEALHNHYTQKLSLSLGLKSGGGGSAPTSSSTKKTQLQLEHLLLDLQMLINGINNYKN PKLTPMLTFKPYMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLELKGSETT FMCEYADETAT IVEFLNRWITFCQSI IISTLT |

TABLE 29-continued

| Sequences | | |
|-----------|--|--|
| SEQ ID | Name | Sequence |
| 489 | 1H3-hIgG4-L6-hIL-2 (D20A/R38S) HC Linker in dashed underline hIL-2 in italics | EVQLVESGGGLVQPGRSLKLSCAVSGFTFSDYAMAWVRQAPKKGLEWVATISYDGSRTYYRDSVKGRFT ISRDNAKITLYLQMDSLRSEDATYYCARHGSGYFDYWGQGMVTVSSASTKGPSVFPPLAPCSRSTSES TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTYYTENVNDRKPS NTKVDKRVESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMIISRTPEVTCVVVDVSDQEDPEVQENWYV DGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDNLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQV YTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSAFLLYSRLTVDKSRW QEGNVFSCSVMHEALHNHYTQKLSLSLGLKSGGGGSAPTSSSTTKKTQLQLEHLLLDLQMLINGINNYKN ----- PKLTSMLTEKFYMPKKATELKHLCLEEEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLELKGSETT FMCEYADETATIVEFLNRWITFCQSIISTLT |
| 490 | 1H3-hIgG4-L6-hIL-2 (D20A/R38D) HC Linker in dashed underline hIL-2 in italics | EVQLVESGGGLVQPGRSLKLSCAVSGFTFSDYAMAWVRQAPKKGLEWVATISYDGSRTYYRDSVKGRFT ISRDNAKITLYLQMDSLRSEDATYYCARHGSGYFDYWGQGMVTVSSASTKGPSVFPPLAPCSRSTSES TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTYYTENVNDRKPS NTKVDKRVESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMIISRTPEVTCVVVDVSDQEDPEVQENWYV DGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDNLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQV YTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSAFLLYSRLTVDKSRW QEGNVFSCSVMHEALHNHYTQKLSLSLGLKSGGGGSAPTSSSTTKKTQLQLEHLLLDLQMLINGINNYKN ----- PKLTDMLTEKFYMPKKATELKHLCLEEEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLELKGSETT FMCEYADETATIVEFLNRWITFCQSIISTLT |
| 491 | 1H3-hIgG4-L6-hIL-2 (D20A/R38Q/E95A) HC Linker in dashed underline hIL-2 in italics | EVQLVESGGGLVQPGRSLKLSCAVSGFTFSDYAMAWVRQAPKKGLEWVATISYDGSRTYYRDSVKGRFT ISRDNAKITLYLQMDSLRSEDATYYCARHGSGYFDYWGQGMVTVSSASTKGPSVFPPLAPCSRSTSES TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTYYTENVNDRKPS NTKVDKRVESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMIISRTPEVTCVVVDVSDQEDPEVQENWYV DGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDNLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQV YTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSAFLLYSRLTVDKSRW QEGNVFSCSVMHEALHNHYTQKLSLSLGLKSGGGGSAPTSSSTTKKTQLQLEHLLLDLQMLINGINNYKN ----- PKLTQMLTFKFYMPKKATELKHLCLEEEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLALKGSETT FMCEYADETATIVEFLNRWITFCQSIISTLT |
| 492 | 1H3-hIgG4-L6-hIL-2 (D20A/F42H/E95A) HC Linker in dashed underline hIL-2 in italics | EVQLVESGGGLVQPGRSLKLSCAVSGFTFSDYAMAWVRQAPKKGLEWVATISYDGSRTYYRDSVKGRFT ISRDNAKITLYLQMDSLRSEDATYYCARHGSGYFDYWGQGMVTVSSASTKGPSVFPPLAPCSRSTSES TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTYYTENVNDRKPS NTKVDKRVESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMIISRTPEVTCVVVDVSDQEDPEVQENWYV DGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDNLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQV YTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSAFLLYSRLTVDKSRW QEGNVFSCSVMHEALHNHYTQKLSLSLGLKSGGGGSAPTSSSTTKKTQLQLEHLLLDLQMLINGINNYKN ----- PKLTRLMLTHKFYMPKKATELKHLCLEEEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLALKGSETT FMCEYADETATIVEFLNRWITFCQSIISTLT |
| 493 | 1H3-hIgG4-L6-hIL-2 (R38D/I92D) HC Linker in dashed underline hIL-2 in italics | EVQLVESGGGLVQPGRSLKLSCAVSGFTFSDYAMAWVRQAPKKGLEWVATISYDGSRTYYRDSVKGRFT ISRDNAKITLYLQMDSLRSEDATYYCARHGSGYFDYWGQGMVTVSSASTKGPSVFPPLAPCSRSTSES TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTYYTENVNDRKPS NTKVDKRVESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMIISRTPEVTCVVVDVSDQEDPEVQENWYV DGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDNLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQV YTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSAFLLYSRLTVDKSRW QEGNVFSCSVMHEALHNHYTQKLSLSLGLKSGGGGSAPTSSSTTKKTQLQLEHLLLDLQMLINGINNYKN ----- PKLTDMLTFKFYMPKKATELKHLCLEEEELKPLEEVLNLAQSKNFHLRPRDLISNINVDVLELKGSETT FMCEYADETATIVEFLNRWITFCQSIISTLT |
| 494 | 1H3-hIgG4-L6-hIL-2 (R38E/I92D) HC Linker in dashed underline hIL-2 in italics | EVQLVESGGGLVQPGRSLKLSCAVSGFTFSDYAMAWVRQAPKKGLEWVATISYDGSRTYYRDSVKGRFT ISRDNAKITLYLQMDSLRSEDATYYCARHGSGYFDYWGQGMVTVSSASTKGPSVFPPLAPCSRSTSES TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTYYTENVNDRKPS NTKVDKRVESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMIISRTPEVTCVVVDVSDQEDPEVQENWYV DGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDNLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQV YTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSAFLLYSRLTVDKSRW QEGNVFSCSVMHEALHNHYTQKLSLSLGLKSGGGGSAPTSSSTTKKTQLQLEHLLLDLQMLINGINNYKN ----- PKLTEMMLTFKFYMPKKATELKHLCLEEEELKPLEEVLNLAQSKNFHLRPRDLISNINVDVLELKGSETT FMCEYADETATIVEFLNRWITFCQSIISTLT |
| 495 | 1H3-hIgG4-L6-hIL-2 (F42H/I92D) HC Linker in | EVQLVESGGGLVQPGRSLKLSCAVSGFTFSDYAMAWVRQAPKKGLEWVATISYDGSRTYYRDSVKGRFT ISRDNAKITLYLQMDSLRSEDATYYCARHGSGYFDYWGQGMVTVSSASTKGPSVFPPLAPCSRSTSES TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTYYTENVNDRKPS NTKVDKRVESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMIISRTPEVTCVVVDVSDQEDPEVQENWYV |

TABLE 29-continued

| Sequences | | |
|------------|--|--|
| SEQ ID NO: | Name | Sequence |
| | dashed | DGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDNLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQV |
| | underline | YTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSRLTVDKSRW |
| | hIL-2 in | QEGNVFSCSVMHEALHNHYTQKLSLSLGGKSGGGGSAPTSSSTKKTQLQLEHLLLDLQMLNGINNYKN |
| | italics | <i>PKLTRLMLTHKFKYMPKKATELKHLCLEEEELKPLEEVLNLAQSKNFHLRPRDLISNINVDVLELKGSETT FMCEYADETATIVEFLNRWITFCQSIISTLT</i> |
| 496 | 1H3-hIgG4-L6-hIL-2 (D20A/R38E) HC Linker in dashed underline | EVQLVESGGGLVQPGRSLKLSCAVSGFTFSDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGRFT ISRDNAKITLYLQMDSLRSEDATYYCARHGSGYFDYWGQGMVTVSSASTKGPSVEPLAPCSRSTSES TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNVDHKPS NTKVDKRVESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMI SRTP EVT CVVVDVSDQEDPEVQENWYV DGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDNLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQV YTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSRLTVDKSRW |
| | hIL-2 in | QEGNVFSCSVMHEALHNHYTQKLSLSLGGKSGGGGSAPTSSSTKKTQLQLEHLLLDLQMLNGINNYKN |
| | italics | <i>PKLTEMLETFKFKYMPKKATELKHLCLEEEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLELKGSETT FMCEYADETATIVEFLNRWITFCQSIISTLT</i> |
| 497 | 1H3-hIgG4-L6-hIL-2 (T3A/D20A/R38E) HC Linker in dashed underline | EVQLVESGGGLVQPGRSLKLSCAVSGFTFSDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGRFT ISRDNAKITLYLQMDSLRSEDATYYCARHGSGYFDYWGQGMVTVSSASTKGPSVEPLAPCSRSTSES TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNVDHKPS NTKVDKRVESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMI SRTP EVT CVVVDVSDQEDPEVQENWYV DGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDNLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQV YTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSRLTVDKSRW |
| | hIL-2 in | QEGNVFSCSVMHEALHNHYTQKLSLSLGGKSGGGGSAPTSSSTKKTQLQLEHLLLDLQMLNGINNYKN |
| | italics | <i>PKLTEMLETFKFKYMPKKATELKHLCLEEEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLELKGSETT FMCEYADETATIVEFLNRWITFCQSIISTLT</i> |
| 498 | 1H3-hIgG4-L6-hIL-2 (D20A/R38E/C125A) HC Linker in dashed underline | EVQLVESGGGLVQPGRSLKLSCAVSGFTFSDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGRFT ISRDNAKITLYLQMDSLRSEDATYYCARHGSGYFDYWGQGMVTVSSASTKGPSVFPPLAPCSRSTSES TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNVDHKPS NTKVDKRVESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMI SRTP EVT CVVVDVSDQEDPEVQENWYV DGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDNLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQV YTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSRLTVDKSRW |
| | hIL-2 in | QEGNVFSCSVMHEALHNHYTQKLSLSLGGKSGGGGSAPTSSSTKKTQLQLEHLLLDLQMLNGINNYKN |
| | italics | <i>PKLTEMLETFKFKYMPKKATELKHLCLEEEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLELKGSETT FMCEYADETATIVEFLNRWITFAQSIISTLT</i> |
| 499 | 1H3-hIgG4-L6-hIL-2 (T3A/D20A/R38E/C125A) HC Linker in dashed underline | EVQLVESGGGLVQPGRSLKLSCAVSGFTFSDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGRFT ISRDNAKITLYLQMDSLRSEDATYYCARHGSGYFDYWGQGMVTVSSASTKGPSVFPPLAPCSRSTSES TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNVDHKPS NTKVDKRVESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMI SRTP EVT CVVVDVSDQEDPEVQENWYV DGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDNLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQV YTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSRLTVDKSRW |
| | hIL-2 in | QEGNVFSCSVMHEALHNHYTQKLSLSLGGKSGGGGSAPTSSSTKKTQLQLEHLLLDLQMLNGINNYKN |
| | italics | <i>PKLTEMLETFKFKYMPKKATELKHLCLEEEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLELKGSETT FMCEYADETATIVEFLNRWITFAQSIISTLT</i> |
| 500 | 1H3-hIgG1-L6-hIL-2 (D20A/R38E) HC Linker in dashed underline | EVQLVESGGGLVQPGRSLKLSCAVSGFTFSDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGRFT ISRDNAKITLYLQMDSLRSEDATYYCARHGSGYFDYWGQGMVTVSSASTKGPSVFPPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPS NTKVDKRVESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMI SRTP EVT CVVVDVSHEDPEVKEN WVVDGVEVHNAKTKPREEQYNSYRVVSVLTVLHQDNLNGKEYKCKVSNKALPAP IEKTI SKAKGQPRE PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSKLTVDK SRWQQGNVFS CSVMHEALHNHYTQKLSLSLPGKSGGGGSELCDDDPPEIPHATFKAMAYKEGTM LNCEC |
| | hIL-2 in | SRWQQGNVFS CSVMHEALHNHYTQKLSLSLPGKSGGGGSELCDDDPPEIPHATFKAMAYKEGTM LNCEC |
| | italics | <i>YKNPKLTEMLETFKFKYMPKKATELKHLCLEEEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLELKGSG ETTEMCEYADETATIVEFLNRWITFCQSIISTLT</i> |
| 501 | 1H3-hIgG1-L6-hIL-2 (T3A/D20A/R38E) HC Linker in dashed underline | EVQLVESGGGLVQPGRSLKLSCAVSGFTFSDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGRET ISRDNAKITLYLQMDSLRSEDATYYCARHGSGYFDYWGQGMVTVSSASTKGPSVFPPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPS NTKVDKRVESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMI SRTP EVT CVVVDVSHEDPEVKEN WVVDGVEVHNAKTKPREEQYNSYRVVSVLTVLHQDNLNGKEYKCKVSNKALPAP IEKTI SKAKGQPRE PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSKLTVDK SRWQQGNVFS CSVMHEALHNHYTQKLSLSLPGKSGGGGSELCDDDPPEIPHATFKAMAYKEGTM LNCEC |
| | hIL-2 in | SRWQQGNVFS CSVMHEALHNHYTQKLSLSLPGKSGGGGSELCDDDPPEIPHATFKAMAYKEGTM LNCEC |
| | italics | <i>YKNPKLTEMLETFKFKYMPKKATELKHLCLEEEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLELKGSG ETTEMCEYADETATIVEFLNRWITFCQSIISTLT</i> |
| 502 | 1H3-hIgG1-L6-hIL-2 (D20A/R38E/C12 | EVQLVESGGGLVQPGRSLKLSCAVSGFTFSDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGRFT ISRDNAKITLYLQMDSLRSEDATYYCARHGSGYFDYWGQGMVTVSSASTKGPSVFPPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPS |

TABLE 29-continued

| Sequences | | |
|------------|--|---|
| SEQ ID NO: | Name | Sequence |
| | 5A) HC Linker in dashed underline | NTKVDKKEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKEN WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPRE PQVYITLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSPFLYSKLTVDK SRWQQGNVFS CVMHEALHNHYTQKLSLSLSPGKSGGGGSELCDDDPEI PHATFKAMAYKEGTM LNCEC |
| | hIL-2 in italics | <i>YKNPKLTEM LTFK F Y M P K K A T E L K H L Q C L E E E L K P L E E V L N L A Q S K N E H L R P R D L I S N I N V I V L E L K G S E T T E M C E Y A D E T A T I V E F L N R W I T F C Q S I I S T L T</i> |
| 503 | 1H3-hKappa-df-hIL-2 (D20A/R38E) LC hIL-2 in italics | DTVLTQSPALAVSPGERVTI SCRASESVRTGVHWYQQKPGQPKLLIYGASNLESVGPARFSGSGSDT FTLTIDPVEADDTATYFCQQSWNDPFTFGSGTKLEIKRTVAAPSVPFIPPPSDEQLKSGTASVCLLNNE YPREAKVQWKVDNALQSGNSQESVTEQDSKSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKS FNRGECAPTSSSTKKTQLQLEHLLALQMI L N G I N N Y K N P K L T E M L T F K F Y M P K K A T E L K H L Q C L E E E L K P L E E V L N L A Q S K N F H L R P R D L I S N I N V I V L E L K G S E T T E M C E Y A D E T A T I V E F L N R W I T F C Q S I I S T L T |
| 504 | 1H3-hKappa-L6-hIL-2 (D20A/R38E) LC Linker in dashed underline hIL-2 in italics | DTVLTQSPALAVSPGERVTI SCRASESVRTGVHWYQQKPGQPKLLIYGASNLESVGPARFSGSGSDT FTLTIDPVEADDTATYFCQQSWNDPFTFGSGTKLEIKRTVAAPSVPFIPPPSDEQLKSGTASVCLLNNE YPREAKVQWKVDNALQSGNSQESVTEQDSKSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKS SRWQQGNVFS CVMHEALHNHYTQKLSLSLSPGKSGGGGSAPTSSSTKKTQLQLEHLLALQMI L N G I N N C L E E E L K P L E E V L N L A Q S K N F H L R P R D L I S N I N V I V L E L K G S E T T E M C E Y A D E T A T I V E F L N R W I T E C Q S I I S T L T |
| 505 | OMC476pB11-hIgG4-df-hIL-2 (D20A/R38E) HC hIL-2 in italics | DVQLVESGGGVVPRGESLRLSCTASGFTFSIAMSWSVRQAPGKGLEWVSAISGTAYSTYYADSVRGRFT ISRDNSKNTLYLQMNLSRAEDTAVYYCAKDNFFDYWGLGTLVTVSSASTKGPSVFPPLAPCSRSTSESTA ALGCLVKDYFPEPVTVSWNSGALTSQVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNVDHKPSNT KVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWYVDG VEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVYIT LPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSPFLYSRLTVDKSRWQE GNVFSCVMHEALHNHYTQKLSLSLKGKAPTSSSTKKTQLQLEHLLALQMI L N G I N N Y K N P K L T E M L T F K F Y M P K K A T E L K H L Q C L E E E L K P L E E V L N L A Q S K N F H L R P R D L I S N I N V I V L E L K G S E T T E M C E Y A D E T A T I V E F L N R W I T F C Q S I I S T L T |
| 506 | OMC476pE4-hIgG4-df-hIL-2 (D20A/R38E) HC hIL-2 in italics | DVQLVESGGGVVPRGESLRLSCTASGFTFSIAMSWSVRQAPGEGLEWVSLISGGYSTYYADSVKGRFT ISRDNSKNTLYLQMNLSRAEDTAVYYCAKNSLAFFDYWGLGTLVTVSSASTKGPSVFPPLAPCSRSTSES TAALGCLVKDYFPEPVTVSWNSGALTSQVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNVDHKPS NTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWYVDG VEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVYIT LPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSPFLYSRLTVDKSRWQE GNVFSCVMHEALHNHYTQKLSLSLKGKAPTSSSTKKTQLQLEHLLALQMI L N G I N N Y K N P K L T E M L T F K F Y M P K K A T E L K H L Q C L E E E L K P L E E V L N L A Q S K N F H L R P R D L I S N I N V I V L E L K G S E T T E M C E Y A D E T A T I V E F L N R W I T F C Q S I I S T L T |
| 507 | OMC476pG10-hIgG4-df-hIL-2 (D20A/R38E) HC hIL-2 in italics | DVQLVESGGGVVPRGGSLRLSCTASGFTFSIAMSWSVRQAPGEGLEWVSHISASGGSTYYADSVKGRFA ISRDNSKNTLYLQMNLSRAEDTAVYYCTTNLGSQDYWGLGTLVTVSSASTKGPSVFPPLAPCSRSTSESTA ALGCLVKDYFPEPVTVSWNSGALTSQVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNVDHKPSNT KVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWYVDG VEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVYIT LPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSPFLYSRLTVDKSRWQE GNVFSCVMHEALHNHYTQKLSLSLKGKAPTSSSTKKTQLQLEHLLALQMI L N G I N N Y K N P K L T E M L T F K F Y M P K K A T E L K H L Q C L E E E L K P L E E V L N L A Q S K N F H L R P R D L I S N I N V I V L E L K G S E T T E M C E Y A D E T A T I V E F L N R W I T F C Q S I I S T L T |
| 508 | OMC476pH10-hIgG4-df-hIL-2 (D20A/R38E) HC hIL-2 in italics | DVQLVESGGGVVPRGGSLRLSCTASGFTFSIAMSWSVRQAPGEGLEWVSHISASGGSTYYADSVKGRFA ISRDNSKNTLYLQMNLSRAEDTAVYYCTTNLGSQDYWGLGTLVTVSSASTKGPSVFPPLAPCSRSTSESTA ALGCLVKDYFPEPVTVSWNSGALTSQVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNVDHKPSNT KVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWYVDG VEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVYIT LPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSPFLYSRLTVDKSRWQE GNVFSCVMHEALHNHYTQKLSLSLKGKAPTSSSTKKTQLQLEHLLALQMI L N G I N N Y K N P K L T E M L T F K F Y M P K K A T E L K H L Q C L E E E L K P L E E V L N L A Q S K N F H L R P R D L I S N I N V I V L E L K G S E T T E M C E Y A D E T A T I V E F L N R W I T F C Q S I I S T L T |
| 509 | A2-hIgG4-df-hIL-2 (D20A/F42A) HC hIL-2 in italics | DVQLVESGGGLVQPGGSLRLSCTASGFTFDIAMSWSVRQAPGKGLEWVSTISGSAYSTYYADSVKGRFT ISRDNSKNTLYLQMNLSRAEDTAVYYCAREIFSDYWGLGTLVTVSSASTKGPSVFPPLAPCSRSTSESTA ALGCLVKDYFPEPVTVSWNSGALTSQVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNVDHKPSNT KVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWYVDG VEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVYIT LPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSPFLYSRLTVDKSRWQE GNVFSCVMHEALHNHYTQKLSLSLKGKAPTSSSTKKTQLQLEHLLALQMI L N G I N N Y K N P K L T E M L T A K F Y M P K K A T E L K H L Q C L E E E L K P L E E V L N L A Q S K N F H L R P R D L I S N I N V I V L E L K G S E T T E M C E Y A D E T A T I V E F L N R W I T F C Q S I I S T L T |

TABLE 29-continued

| Sequences | | |
|------------|--|--|
| SEQ ID NO: | Name | Sequence |
| 510 | A2-hIgG4-df-hIL-2 (D20A/F42S) HC hIL-2 in <i>italics</i> | DVQLVESGGGLVQPGGSLRLSCAASGFTFDISAMSWVRQAPGKGLEWVSTISGSAYSTYYADSVKGRETISRDNKSTLYLQMNSLRAEDTAVYYCAREIFSDYWGLGTLVTVSSASTKGPSVFPPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSRLTVDKSRWQEGNVFSCVMHEALHNHYTQKLSLSLGKAPTSSSTKKTQLQLEHLLLDLQMI LNGINNYKPKLTRMLTKFYMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLISININVDVLELKGSETTEMCEYADETATIVEFLNRWITFCQSIISTLT |
| 511 | A2-hIgG4-df-hIL-2 (D20S/R38E) HC hIL-2 in <i>italics</i> | DVQLVESGGGLVQPGGSLRLSCAASGFTFDISAMSWVRQAPGKGLEWVSTISGSAYSTYYADSVKGRFTISRDNKSTLYLQMNSLRAEDTAVYYCAREIFSDYWGLGTLVTVSSASTKGPSVFPPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSRLTVDKSRWQEGNVFSCVMHEALHNHYTQKLSLSLGKAPTSSSTKKTQLQLEHLLLDLQMI LNGINNYKPKLTRMLTKFYMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLISININVDVLELKGSETTEMCEYADETATIVEFLNRWITFCQSIISTLT |
| 512 | A2-hIgG4-df-hIL-2 (F42A/N88R) HC hIL-2 in <i>italics</i> | DVQLVESGGGLVQPGGSLRLSCAASGFTFDISAMSWVRQAPGKGLEWVSTISGSAYSTYYADSVKGRFTISRDNKSTLYLQMNSLRAEDTAVYYCAREIFSDYWGLGTLVTVSSASTKGPSVFPPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSRLTVDKSRWQEGNVFSCVMHEALHNHYTQKLSLSLGKAPTSSSTKKTQLQLEHLLLDLQMI LNGINNYKPKLTRMLTKAFYMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLISININVDVLELKGSETTEMCEYADETATIVEFLNRWITFCQSIISTLT |
| 513 | A2-hIgG4-df-hIL-2 (F42I/I92D) HC hIL-2 in <i>italics</i> | DVQLVESGGGLVQPGGSLRLSCAASGFTFDISAMSWVRQAPGKGLEWVSTISGSAYSTYYADSVKGRFTISRDNKSTLYLQMNSLRAEDTAVYYCAREIFSDYWGLGTLVTVSSASTKGPSVFPPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSRLTVDKSRWQEGNVFSCVMHEALHNHYTQKLSLSLGKAPTSSSTKKTQLQLEHLLLDLQMI LNGINNYKPKLTRMLTKFYMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLISININVDVLELKGSETTEMCEYADETATIVEFLNRWITFCQSIISTLT |
| 514 | A2-hIgG4-df-hIL-2 (F42Q/I92D) HC hIL-2 in <i>italics</i> | DVQLVESGGGLVQPGGSLRLSCAASGFTFDISAMSWVRQAPGKGLEWVSTISGSAYSTYYADSVKGRFTISRDNKSTLYLQMNSLRAEDTAVYYCAREIFSDYWGLGTLVTVSSASTKGPSVFPPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSRLTVDKSRWQEGNVFSCVMHEALHNHYTQKLSLSLGKAPTSSSTKKTQLQLEHLLLDLQMI LNGINNYKPKLTRMLTKFYMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLISININVDVLELKGSETTEMCEYADETATIVEFLNRWITFCQSIISTLT |
| 515 | A2-hIgG4-df-hIL-2 (F42T/I92D) HC hIL-2 in <i>italics</i> | DVQLVESGGGLVQPGGSLRLSCAASGFTFDISAMSWVRQAPGKGLEWVSTISGSAYSTYYADSVKGRFTISRDNKSTLYLQMNSLRAEDTAVYYCAREIFSDYWGLGTLVTVSSASTKGPSVFPPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSRLTVDKSRWQEGNVFSCVMHEALHNHYTQKLSLSLGKAPTSSSTKKTQLQLEHLLLDLQMI LNGINNYKPKLTRMLTKFYMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLISININVDVLELKGSETTEMCEYADETATIVEFLNRWITFCQSIISTLT |
| 516 | A2-hIgG4-df-hIL-2 (F42W/I92D) HC hIL-2 in <i>italics</i> | DVQLVESGGGLVQPGGSLRLSCAASGFTFDISAMSWVRQAPGKGLEWVSTISGSAYSTYYADSVKGRFTISRDNKSTLYLQMNSLRAEDTAVYYCAREIFSDYWGLGTLVTVSSASTKGPSVFPPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSRLTVDKSRWQEGNVFSCVMHEALHNHYTQKLSLSLGKAPTSSSTKKTQLQLEHLLLDLQMI LNGINNYKPKLTRMLTKFYMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLISININVDVLELKGSETTEMCEYADETATIVEFLNRWITFCQSIISTLT |
| 517 | A2-hIgG4-df-hIL-2 (R38E/D84K) HC hIL-2 in <i>italics</i> | DVQLVESGGGLVQPGGSLRLSCAASGFTFDISAMSWVRQAPGKGLEWVSTISGSAYSTYYADSVKGRFTISRDNKSTLYLQMNSLRAEDTAVYYCAREIFSDYWGLGTLVTVSSASTKGPSVFPPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSRLTVDKSRWQEGNVFSCVMHEALHNHYTQKLSLSLGKAPTSSSTKKTQLQLEHLLLDLQMI LNGINNYKPKLTRMLTKFYMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLISININVDVLELKGSETTEMCEYADETATIVEFLNRWITFCQSIISTLT |

TABLE 29-continued

| Sequences | | |
|------------|--|---|
| SEQ ID NO: | Name | Sequence |
| | | LPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRLTVDKSRWQE GNVFSCSVMHEALHNHYTQKSLSLGLKAPTSSSTKKTQLQLEHLLLDLQMI LINGINNYKNPKLTEM LTKFYMFKKATELKHLCLEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLELKGSETTEM CEYADETATIVEFLNRWITFCQSIISTLT |
| 518 | A2-hIgG4-df-hIL-2 (R38E/192K) HC hIL-2 in italics | DVQLVESGGGLVQPGGSLRLSCAASGFTFDISAMSWVRQAPGKGLEWVSTISGSAYSTYYADSVKGRFT ISRDNKSTLYLQMNLSRAEDTAVYYCAREIFSDYWGGLGLVTVSSASTKGPSVEPLAPCSRSTSESTA ALGCLVKDYFPEPVTVSWNSGALTSVHTFPAPVQLQSSGLYSLSSVTVPSSSLGKTYTCNVDDHKPSNT KVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWVVDG VEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVY LPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRLTVDKSRWQE GNVFSCSVMHEALHNHYTQKSLSLGLKAPTSSSTKKTQLQLEHLLLDLQMI LINGINNYKNPKLTEM LTKFYMFKKATELKHLCLEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLELKGSETTEM CEYADETATIVEFLNRWITFCQSIISTLT |
| 519 | C51E6-5-hIgG4-df-hIL-2 (D20A/R38E) HC hIL-2 in italics | QVQLVQSGSELEKPKGASVKVSKASGYSLYGTSMHWVRQAPGGLEWVMGYISPFTGRATYAQGFTGREV FSLDTSVSTAYLQISSLKAEDTAVYYCARDYDYYRYAMDYWGQGTTVTVSSASTKGPSVFLAPCSR TSESTAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAPVQLQSSGLYSLSSVTVPSSSLGKTYTCNV DHPKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQ FNWVVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQ PREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRLTV DKSRWQEGNVFSCVMHEALHNHYTQKSLSLGLKAPTSSSTKKTQLQLEHLLLDLQMI LINGINNYKNPK LTEM LTKFYMFKKATELKHLCLEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLELKGSETTEM CEYADETATIVEFLNRWITFCQSIISTLT |
| 520 | C51E6-5-hIgG4-LE-df-hIL-2 (T3A/D20A/R38E/ C125A) HC hIL-2 in italics | QVQLVQSGSELEKPKGASVKVSKASGYSLYGTSMHWVRQAPGGLEWVMGYISPFTGRATYAQGFTGREV FSLDTSVSTAYLQISSLKAEDTAVYYCARDYDYYRYAMDYWGQGTTVTVSSASTKGPSVFLAPCSR TSESTAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAPVQLQSSGLYSLSSVTVPSSSLGKTYTCNV DHPKPSNTKVDKRVESKYGPPCPPCPAPEFEGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQ FNWVVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQ PREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRLTV DKSRWQEGNVFSCVMHEALHNHYTQKSLSLGLKAPASSSTKKTQLQLEHLLLDLQMI LINGINNYKNPK LTEM LTKFYMFKKATELKHLCLEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLELKGSETTEM CEYADETATIVEFLNRWITFAQSIISTLT |
| 521 | C51E6-5-hIgG4-LAGA-df-hIL-2 (T3A/D20A/R38E/ C125A) HC hIL-2 in italics | QVQLVQSGSELEKPKGASVKVSKASGYSLYGTSMHWVRQAPGGLEWVMGYISPFTGRATYAQGFTGREV FSLDTSVSTAYLQISSLKAEDTAVYYCARDYDYYRYAMDYWGQGTTVTVSSASTKGPSVFLAPCSR TSESTAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAPVQLQSSGLYSLSSVTVPSSSLGKTYTCNV DHPKPSNTKVDKRVESKYGPPCPPCPAPEFAGAPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQ FNWVVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQ PREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRLTV DKSRWQEGNVFSCVMHEALHNHYTQKSLSLGLKAPASSSTKKTQLQLEHLLLDLQMI LINGINNYKNPK LTEM LTKFYMFKKATELKHLCLEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLELKGSETTEM CEYADETATIVEFLNRWITFAQSIISTLT |
| 522 | 1H3-hIgG1-LAGA-L6-hIL-2 (T3A/D20A/R38E/ C125A) | EVQLVESGGGLVQPGGSLRLSCAVSGFTFSDYAMAWVRQAPKKGLEWVATISYDGSRTYYRDSVVKGRFT ISRDNKSTLYLQMNLSRAEDTAVYYCARHSGYFDYWGQGMVTVSSASTKGPSVFLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAPVQLQSSGLYSLSSVTVPSSSLGTYTCNV DHPKPSNTKVDKRVESKYGPPCPPCPAPELAGAPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVK ENWVVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI SKAKGQ PREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRLTV DKSRWQEGNVFSCVMHEALHNHYTQKSLSLSPKSGGGGAPASSSTKKTQLQLEHLLLDLQMI LINGIN NYKNPKLTEM LTKFYMFKKATELKHLCLEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLELKG SETTEMCEYADETATIVEFLNRWITFAQSIISTLT |
| 523 | 2A3-hKappa LC | EIVLTQSPGTLSLSPGERATLSCRASQSIGRSFLAWYQQKPGQAPRLLIYDASTRAADI PARFSGSGG TDFTLTISSLEPEDFAVYYCQQYDWPPLSFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVCLL NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSYSLSSLTLSKADYEEKHKVYACEVTHQGLSSPV TKSENREGE |
| 524 | 1H9-hIgG4-df-hIL-2 (D20A/R38E) HC hIL-2 in italics | EVQLLESGGGLVQPGGSLRLSCVGSFNLKDYCMTWVRQAPKKGLEWVSAIVYSGGSTYYADSVKGRFT ISRDNKSTLYLQMNLSRAEDTAVYYCAKTRGSYFDYDAMDYWGQGTTVTVSSASTKGPSVFLAPCSR STSESTAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAPVQLQSSGLYSLSSVTVPSSSLGKTYTCNV DHPKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQ FNWVVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQ PREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRLTV DKSRWQEGNVFSCVMHEALHNHYTQKSLSLGLKAPTSSSTKKTQLQLEHLLLDLQMI LINGINNYKNPK LTEM LTKFYMFKKATELKHLCLEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLELKGSETTE MCEYADETATIVEFLNRWITFCQSIISTLT |
| 525 | 1H9-hkappa LC | EIVLTQSPGTLSLSPGERATLSCRASQSIGRSFLAWYQQKPGQAPRLLIYDASTRAADIPDRESGSGG TDFTLTINRLEPEDFAVYYCQQYDWPPLTFGGGKVEIKRTVAAPSVFIFPPSDEQLKSGTASVCLL NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSYSLSSLTLSKADYEEKHKVYACEVTHQGLSSPV TKSENREGE |

TABLE 29-continued

| Sequences | | |
|------------|--|---|
| SEQ ID NO: | Name | Sequence |
| 526 | 1D5-hIgG4-df-hIL-2 (D20A/R38E) HC hIL-2 in <i>italics</i> | EVQLLESGGGLVQPGGSLRLSCVGSNGENFKDYCMTWVRQAPGKGLEWVSAIVYSGGSTYYADSVKGRET ISRDNKNTLYLQMNLSRAEDTAVYYCAKYTRGSYFYDAMDVWGQGTTVTVSSASTKGPSVFLPAPCSR STSESTAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSVTVTPSSSLGKTKYTCNV DHKPSNTKVDKRVESKYGPPCPPAPEFLGGPSVLEFPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQ FNWYVDGVEVHNAKTKPREEQPNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI S KAKGQP REPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRLTV DKSRWQEGNVFSCVMHEALHNYHTQKSLSLSLGKAPASSSTKTKTQLQLEHLLALQMLINGINNYKNP KLTEMLTFKFFYMPKKATELKHLCLEELKPLEEVLNLAQSKNFHLRPRDLI SNINVI VLELKGSETTE MCEYADETATIVFELNRWITFAQSIISTLT |
| 527 | 1D5-hKappa LC | EIVLTQSPGTLSLSPGERATLSCRASQSIGRSLFLAWYQQKPGQAPRLLIYDASTRATDI PDRESGSGSG TEFTLTISSLQSEDFAVYYCQQYDWPPLTFGGGTKEVEIKRTVAAPSVFIFPPSDQLKSGTASVVCLL NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSYSLSSLTTLTKADYEKHKVYACEVTHQGLSSPV TKSENREGEC |
| 528 | 1D5-hIgG4-LE-df-hIL-2 (T3A/D20A/R38E/C125A) HC hIL-2 in <i>italics</i> | EVQLLESGGGLVQPGGSLRLSCVGSNGENFKDYCMTWVRQAPGKGLEWVSAIVYSGGSTYYADSVKGRFT ISRDNKNTLYLQMNLSRAEDTAVYYCAKYTRGSYFYDAMDVWGQGTTVTVSSASTKGPSVFLPAPCSR STSESTAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSVTVTPSSSLGKTKYTCNV DHKPSNTKVDKRVESKYGPPCPPAPEFEGGPSVLEFPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQ FNWYVDGVEVHNAKTKPREEQPNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI S KAKGQP REPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRLTV DKSRWQEGNVFSCVMHEALHNYHTQKSLSLSLGKAPASSSTKTKTQLQLEHLLALQMLINGINNYKNP KLTEMLTFKFFYMPKKATELKHLCLEELKPLEEVLNLAQSKNFHLRPRDLI SNINVI VLELKGSETTE MCEYADETATIVFELNRWITFAQSIISTLT |
| 529 | 1D5-hIgG4-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) HC hIL-2 in <i>italics</i> | EVQLLESGGGLVQPGGSLRLSCVGSNGENFKDYCMTWVRQAPGKGLEWVSAIVYSGGSTYYADSVKGRET ISRDNKNTLYLQMNLSRAEDTAVYYCAKYTRGSYFYDAMDVWGQGTTVTVSSASTKGPSVFLPAPCSR STSESTAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSVTVTPSSSLGKTKYTCNV DHKPSNTKVDKRVESKYGPPCPPAPEFAGAPSVLEFPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQ FNWYVDGVEVHNAKTKPREEQPNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI S KAKGQP REPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRLTV DKSRWQEGNVFSCVMHEALHNYHTQKSLSLSLGKAPASSSTKTKTQLQLEHLLALQMLINGINNYKNP KLTEMLTFKFFYMPKKATELKHLCLEELKPLEEVLNLAQSKNFHLRPRDLI SNINVI VLELKGSETTE MCEYADETATIVFELNRWITFAQSIISTLT |
| 530 | 2H7-hIgG1-df-hIL-2 (T3A/D20A/R38E/C125A) HC hIL-2 in <i>italics</i> | EVQLLESGGGLVQPGGSLRLSCAASGFTFKDYCMTWVRQAPGKGLEWVSAIVYSGGSTYYADSVKGRFT ISRDNKNTLYLQMNLSRAEDTAVYYCAKYTRASYFYDAMDVWGQGTTVTVSSASTKGPSVFLPAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSVTVTPSSSLGKTKYTCNV NHKPSNTKVDKRVESKYGPPCPPAPEFLGGPSVLEFPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQ FNWYVDGVEVHNAKTKPREEQPNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI S KAKGQP REPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSK LTVDKSRWQEGNVFSCVMHEALHNYHTQKSLSLSLGKAPASSSTKTKTQLQLEHLLALQMLINGINNY KNPKL TEMLTFKFFYMPKKATELKHLCLEELKPLEEVLNLAQSKNFHLRPRDLI SNINVI VLELKGSE TTFMCEYADETATIVFELNRWITFAQSIISTLT |
| 531 | 2H7-hIgG1-LE-df-hIL-2 (T3A/D20A/R38E/C125A) HC hIL-2 in <i>italics</i> | EVQLLESGGGLVQPGGSLRLSCAASGFTFKDYCMTWVRQAPGKGLEWVSAIVYSGGSTYYADSVKGRFT ISRDNKNTLYLQMNLSRAEDTAVYYCAKYTRASYFYDAMDVWGQGTTVTVSSASTKGPSVFLPAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSVTVTPSSSLGKTKYTCNV NHKPSNTKVDKRVESKYGPPCPPAPELEGGPSVLEFPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQ FNWYVDGVEVHNAKTKPREEQPNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI S KAKGQP REPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSK LTVDKSRWQEGNVFSCVMHEALHNYHTQKSLSLSLGKAPASSSTKTKTQLQLEHLLALQMLINGINNY KNPKL TEMLTFKFFYMPKKATELKHLCLEELKPLEEVLNLAQSKNFHLRPRDLI SNINVI VLELKGSE TTFMCEYADETATIVFELNRWITFAQSIISTLT |
| 532 | H7-767 HC | EVQLLESGGGLVQPGGSLRLSCAASGFTFKSYAMHWVRQAPGKGLEWVSAIVYSGGSTYYADSVKGRFT ISRDNKNTLYLQMNLSRAEDTAVYYCAKYDRASYFYDAMDVWGQGTTVTVSSASTKGPSVFLPAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSVTVTPSSSLGKTKYTCNV NHKPSNTKVDKRVESKYGPPCPPAPELAGAPSVLEFPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQ FNWYVDGVEVHNAKTKPREEQPNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI S KAKGQP REPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSK LTVDKSRWQEGNVFSCVMHEALHNYHTQKSLSLSLGKAPASSSTKTKTQLQLEHLLALQMLINGINNY KNPKL TEMLTFKFFYMPKKATELKHLCLEELKPLEEVLNLAQSKNFHLRPRDLI SNINVI VLELKGSE TTFMCEYADETATIVFELNRWITFAQSIISTLT |
| 533 | 2H7-hIgG1-LE-df-hIL-2 (T3A/R38E/D84K/C125A) HC hIL-2 in <i>italics</i> | EVQLLESGGGLVQPGGSLRLSCAASGFTFKDYCMTWVRQAPGKGLEWVSAIVYSGGSTYYADSVKGRFT ISRDNKNTLYLQMNLSRAEDTAVYYCAKYTRASYFYDAMDVWGQGTTVTVSSASTKGPSVFLPAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSVTVTPSSSLGKTKYTCNV NHKPSNTKVDKRVESKYGPPCPPAPELEGGPSVLEFPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQ FNWYVDGVEVHNAKTKPREEQPNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI S KAKGQP REPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSK LTVDKSRWQEGNVFSCVMHEALHNYHTQKSLSLSLGKAPASSSTKTKTQLQLEHLLALQMLINGINNY KNPKL TEMLTFKFFYMPKKATELKHLCLEELKPLEEVLNLAQSKNFHLRPRDLI SNINVI VLELKGSE TTFMCEYADETATIVFELNRWITFAQSIISTLT |

TABLE 29-continued

| Sequences | | |
|------------|---|--|
| SEQ ID NO: | Name | Sequence |
| 534 | 2H7-hIgG4-df-hIL-2 (T3A/R38E/D84K/C125A) HC hIL-2 in italics | EVQLLESGGGLVQPGGSLRLSCAASGFTFKDYCMTWVRQAPGKGLEWVSAIVYSGGSTYYADSVKGRFT ISRDNKNTLYLQMNLRADTAVYYCAKYTRASYFYDAMDVWGQTTVTVSSASTKGPSVEFLAPCSR STSESTAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSVVTVPSSSLGTQTYICNV DHKPSNTKVDKRVESKYGPPCPPCPAPELGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQ FNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYCKVSNKGLPSSIEKTI SKAKGQP RPEQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSAFLLYSK DKSRWQEGNVFSCVMHEALHNHYTQKSLSLSPGKAPASSSTKTKTQLQLEHLLLDLQMI LINGINNY KLTEMLTFKGYMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLI SNINVI VLELKGSETTE MCEYADETATIV EFLNRWITFAQSII STLT |
| 535 | 2H7-hIgG1-df-hIL-2 (T3A/R38E/192K/C125A) HC hIL-2 in italics | EVQLLESGGGLVQPGGSLRLSCAASGFTFKDYCMTWVRQAPGKGLEWVSAIVYSGGSTYYADSVKGRFT ISRDNKNTLYLQMNLRADTAVYYCAKYTRASYFYDAMDVWGQTTVTVSSASTKGPSVFPPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSVVTVPSSSLGTQTYICNV NHKPSNTKVDKKEPKSCDKTHTCPPCPAPELGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPI EKTISKAK GQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSAFLLYSK LTVDKSRWQEGNVFSCVMHEALHNHYTQKSLSLSPGKAPASSSTKTKTQLQLEHLLLDLQMI LINGINNY KNPKL TEMLTFKGYMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLI SNINVKVLELKGSE TTFMCEYADETATIV EFLNRWITFAQSII STLT |
| 536 | 2H7-hIgG1-LE-df-hIL-2 (T3A/R38E/192K/C125A) HC hIL-2 in italics | EVQLLESGGGLVQPGGSLRLSCAASGFTFKDYCMTWVRQAPGKGLEWVSAIVYSGGSTYYADSVKGRFT ISRDNKNTLYLQMNLRADTAVYYCAKYTRASYFYDAMDVWGQTTVTVSSASTKGPSVFPPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSVVTVPSSSLGTQTYICNV NHKPSNTKVDKKEPKSCDKTHTCPPCPAPELGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPI EKTISKAK GQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSAFLLYSK LTVDKSRWQEGNVFSCVMHEALHNHYTQKSLSLSPGKAPASSSTKTKTQLQLEHLLLDLQMI LINGINNY KNPKL TEMLTFKGYMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLI SNINVKVLELKGSE TTFMCEYADETATIV EFLNRWITFAQSII STLT |
| 537 | 2H7-hIgG4-df-hIL-2 (T3A/R38E/192K/C125A) HC hIL-2 in italics | EVQLLESGGGLVQPGGSLRLSCAASGFTFKDYCMTWVRQAPGKGLEWVSAIVYSGGSTYYADSVKGRFT ISRDNKNTLYLQMNLRADTAVYYCAKYTRASYFYDAMDVWGQTTVTVSSASTKGPSVEFLAPCSR STSESTAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSVVTVPSSSLGTQTYICNV DHKPSNTKVDKRVESKYGPPCPPCPAPELGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQ FNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYCKVSNKGLPSSIEKTI SKAKGQP RPEQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSAFLLYSK DKSRWQEGNVFSCVMHEALHNHYTQKSLSLSPGKAPASSSTKTKTQLQLEHLLLDLQMI LINGINNY KLTEMLTFKGYMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLI SNINVI VLELKGSETTE MCEYADETATIV EFLNRWITFAQSII STLT |
| 538 | 2H7-hIgG1-LAGA-df-hIL2 (T3A/D20S/R38E/C125A) HC hIL-2 in italics | EVQLLESGGGLVQPGGSLRLSCAASGFTFKDYCMTWVRQAPGKGLEWVSAIVYSGGSTYYADSVKGRFT ISRDNKNTLYLQMNLRADTAVYYCAKYTRASYFYDAMDVWGQTTVTVSSASTKGPSVFPPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSVVTVPSSSLGTQTYICNV NHKPSNTKVDKKEPKSCDKTHTCPPCPAPELAGAPSVLFPKPKDTLMI SRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPI EKTISKAK GQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSAFLLYSK LTVDKSRWQEGNVFSCVMHEALHNHYTQKSLSLSPGKAPASSSTKTKTQLQLEHLLLDLQMI LINGINNY KNPKL TEMLTFKGYMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLI SNINVI VLELKGSE TTFMCEYADETATIV EFLNRWITFAQSII STLT |
| 539 | 2H7-hIgG1-LAGA-df-hIL2 (T3A/R38E/D84F/C125A) HC hIL-2 in italics | EVQLLESGGGLVQPGGSLRLSCAASGFTFKDYCMTWVRQAPGKGLEWVSAIVYSGGSTYYADSVKGRFT ISRDNKNTLYLQMNLRADTAVYYCAKYTRASYFYDAMDVWGQTTVTVSSASTKGPSVFPPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSVVTVPSSSLGTQTYICNV NHKPSNTKVDKKEPKSCDKTHTCPPCPAPELAGAPSVLFPKPKDTLMI SRTPEVTCVVVDVSHEDP EVKENWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPI EKTISKAK GQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSAFLLYSK LTVDKSRWQEGNVFSCVMHEALHNHYTQKSLSLSPGKAPASSSTKTKTQLQLEHLLLDLQMI LINGINNY KNPKL TEMLTFKGYMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLI SNINVI VLELKGSE TTFMCEYADETATIV EFLNRWITFAQSII STLT |
| 540 | 2H7-hIgG1-LAGA-df-hIL2 (T3A/R38E/192R/C125A) HC hIL-2 in italics | EVQLLESGGGLVQPGGSLRLSCAASGFTFKDYCMTWVRQAPGKGLEWVSAIVYSGGSTYYADSVKGRFT ISRDNKNTLYLQMNLRADTAVYYCAKYTRASYFYDAMDVWGQTTVTVSSASTKGPSVFPPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSVVTVPSSSLGTQTYICNV NHKPSNTKVDKKEPKSCDKTHTCPPCPAPELAGAPSVLFPKPKDTLMI SRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPI EKTISKAK GQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSAFLLYSK LTVDKSRWQEGNVFSCVMHEALHNHYTQKSLSLSPGKAPASSSTKTKTQLQLEHLLLDLQMI LINGINNY KNPKL TEMLTFKGYMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLI SNINVRVLELKGSE TTFMCEYADETATIV EFLNRWITFAQSII STLT |

TABLE 29-continued

| Sequences | | |
|------------|---|---|
| SEQ ID NO: | Name | Sequence |
| 541 | 2H7-hIgG1-LAGA-df-hIL2 (T3A/R38E/I92E/C125A) HC hIL-2 in italics | EVQLLESGGGLVQPGGSLRLSCAASGFTFKDYCMTWVRQAPGKGLEWVSAIVYSGGSTYIADSVKGRET ISRDN SKNTLYLQMNLR AEDTAVYYCAKYTRASYFYDAMDVWGQGT TTVTVSSASTKGPSVFP LAPSSK STSGGTAALGCLVKDYFPEPVT VSWNSGALTS GVHTFPAVLQSSGLYSLSVVTVPSSSLGTQTYICNV NHKPSNTKVDK KVEPKSCDKTHTCPPCPAPELAGAPSVELFPPKPKDTLMISRTPEVTCVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI SKAK GQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDG SFFLYSK LTVDKSRWQQGNV FSCVMHEALHNHYTQKSLSLSPGKAPASSSTKKTQLQLEHLLLDLQMI LINGINNY KNPKLTEM LTFKFYMPK KATEL KHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLI SNINVEVLELKGSE TTFMCEYADETAT IVEFLNRWITFAQSIISTLT |
| 542 | 2H7-hIgG1-LAGA-df-hIL2 (T3A/R38E/I92S/C125A) HC hIL-2 in italics | EVQLLESGGGLVQPGGSLRLSCAASGFTFKDYCMTWVRQAPGKGLEWVSAIVYSGGSTYIADSVKGRET ISRDN SKNTLYLQMNLR AEDTAVYYCAKYTRASYFYDAMDVWGQGT TTVTVSSASTKGPSVFP LAPSSK STSGGTAALGCLVKDYFPEPVT VSWNSGALTS GVHTFPAVLQSSGLYSLSVVTVPSSSLGTQTYICNV NHKPSNTKVDK KVEPKSCDKTHTCPPCPAPELAGAPSVELFPPKPKDTLMISRTPEVTCVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI SKAK GQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDG SFFLYSK LTVDKSRWQQGNV FSCVMHEALHNHYTQKSLSLSPGKAPASSSTKKTQLQLEHLLLDLQMI LINGINNY KNPKLTEM LTFKFYMPK KATEL KHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLI SNINVEVLELKGSE TTFMCEYADETAT IVEFLNRWITFAQSIISTLT |
| 543 | 2H7-hIgG1-LAGA-df-hIL2 (T3A/R38E/I92D/C125A) HC hIL-2 in italics | EVQLLESGGGLVQPGGSLRLSCAASGFTFKDYCMTWVRQAPGKGLEWVSAIVYSGGSTYIADSVKGRET ISRDN SKNTLYLQMNLR AEDTAVYYCAKYTRASYFYDAMDVWGQGT TTVTVSSASTKGPSVFP LAPSSK STSGGTAALGCLVKDYFPEPVT VSWNSGALTS GVHTFPAVLQSSGLYSLSVVTVPSSSLGTQTYICNV NHKPSNTKVDK KVEPKSCDKTHTCPPCPAPELAGAPSVELFPPKPKDTLMISRTPEVTCVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI SKAK GQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDG SFFLYSK LTVDKSRWQQGNV FSCVMHEALHNHYTQKSLSLSPGKAPASSSTKKTQLQLEHLLLDLQMI LINGINNY KNPKLTEM LTFKFYMPK KATEL KHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLI SNINVEVLELKGSE TTFMCEYADETAT IVEFLNRWITFAQSIISTLT |
| 544 | 2H7-hIgG1-LAGA-df-hIL2 (T3A/H16E/R38E/C125A) HC hIL-2 in italics | EVQLLESGGGLVQPGGSLRLSCAASGFTFKDYCMTWVRQAPGKGLEWVSAIVYSGGSTYIADSVKGRET ISRDN SKNTLYLQMNLR AEDTAVYYCAKYTRASYFYDAMDVWGQGT TTVTVSSASTKGPSVFP LAPSSK STSGGTAALGCLVKDYFPEPVT VSWNSGALTS GVHTFPAVLQSSGLYSLSVVTVPSSSLGTQTYICNV NHKPSNTKVDK KVEPKSCDKTHTCPPCPAPELAGAPSVELFPPKPKDTLMISRTPEVTCVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI SKAK GQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDG SFFLYSK LTVDKSRWQQGNV FSCVMHEALHNHYTQKSLSLSPGKAPASSSTKKTQLQLEEELLDLQMI LINGINNY KNPKLTEM LTFKFYMPK KATEL KHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLI SNINVI VLELKGSE TTFMCEYADETAT IVEFLNRWITFAQSIISTLT |
| 545 | 1H3-hIgG1-L6-hIL-2 (T3A/D20A/R38E/C125A) HC Linker in dashed underline hIL-2 in italics | EVQLVESGGGLVQPGRSLKLSCAVSGFTFSDYAMAWVRQAPK KGLEWVATISYDGSRTYYRDSVKGRFT ISRDN AKITLYLQMDSLRSED TATYYCARHSGSYFDYWGQGMVTVSSASTKGPSVFP LAPSSKSTSGG TAALGCLVKDYFPEPVT VSWNSGALTS GVHTFPAVLQSSGLYSLSVVTVPSSSLGTQTYICNVNHKPS NTKVDK KVEPKSCDKTHTCPPCPAPELLGGPSVLEFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKEN WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI SKAKGQPRE PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDG SFFLYSKLTVDK SRWQQGNV FSCVMHEALHNHYTQKSLSLSPGKSGGGGSELCDDDPPEI PHATFKAMAYKEGTM LNCEC YKNPKLTEM LTFKFYMPK KATEL KHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLI SNINVI VLELKGSE ETTEMCEYADETAT IVEFLNRWITFAQSIISTLT |
| 546 | 1H3-hIgG1-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) HC hIL-2 in italics | EVQLVESGGGLVQPGRSLKLSCAVSGFTFSDYAMAWVRQAPK KGLEWVATISYDGSRTYYRDSVKGRFT ISRDN AKITLYLQMDSLRSED TATYYCARHSGSYFDYWGQGMVTVSSASTKGPSVFP LAPSSKSTSGG TAALGCLVKDYFPEPVT VSWNSGALTS GVHTFPAVLQSSGLYSLSVVTVPSSSLGTQTYICNVNHKPS NTKVDK KVEPKSCDKTHTCPPCPAPELLGGPSVLEFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKEN WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI SKAKGQPRE PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDG SFFLYSKLTVDK SRWQQGNV FSCVMHEALHNHYTQKSLSLSPGKAPASSSTKKTQLQLEHLLLDLQMI LINGINNYKNPKL TEM LTFKFYMPK KATEL KHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLI SNINVI VLELKGSE EYADETATI VEFNLNRWITFAQSIISTLT |
| 547 | C51E6-5-hIgG4/k-LE HC | QVQLVQSGSELKPGASVKVSKASGYSLYGTSMHWVRQAPGQGLEWMGYIS PPTGRATYAQGTGREV FSLDTSVSTAYLQISSLKAEDTAVYYCARDYDYRYYYAMDYWGQGT TTVTVSSASTKGPSVFP LAPCSR TSBSTAALGCLVKDYFPEPVT VSWNSGALTS GVHTFPAVLQSSGLYSLSVVTVPSSSLGTQTYICNV HKPSNTKVDKRVESKYGPPCPPCPAPEFEGGSPVELFPPKPKDTLMISRTPEVTCVVDVSDQEDPEVQF WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI SKAKGQPRE EPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDG SFFLYSRLTVD KSRWQEGNV FSCVMHEALHNHYTQKSLSLSLG |

TABLE 29-continued

| Sequences | | |
|------------|--|---|
| SEQ ID NO: | Name | Sequence |
| 548 | C51E6-5-hIgG4/k-LAGA HC | QVQLVQSGSELKPKGASVKVSKASGYSLYGTSMHWVRQAPGGLEWVMGYISPFTRGRATYAQGFTGREV FSLDTSVSTAYLQISSLKAEDTAVYYCARDYDYYRYYYAMDYWGQGT TVTVSSASTKGPSVEPLAPCSRST TSESTAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSVTVPSSSLGKTKYTCNVDD HKPSNTKVDKRVESKYGPPCPPCPAPEFAGAPSVLEFPKPKDTLMISRTPEVTCVVVDVSDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPR EPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVD KSRWQEGNVFSCVMHEALHNHYTQKLSLSLGLG |
| 549 | C51E6-5-hIgG4/k-LEPG HC | QVQLVQSGSELKPKGASVKVSKASGYSLYGTSMHWVRQAPGGLEWVMGYISPFTRGRATYAQGFTGREV FSLDTSVSTAYLQISSLKAEDTAVYYCARDYDYYRYYYAMDYWGQGT TVTVSSASTKGPSVFPPLAPCSRST TSESTAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSVTVPSSSLGKTKYTCNVDD HKPSNTKVDKRVESKYGPPCPPCPAPEFEGGPSVLEFPKPKDTLMISRTPEVTCVVVDVSDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLGSSIEKTI SKAKGQPR EPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVD KSRWQEGNVFSCVMHEALHNHYTQKLSLSLGLG |
| 550 | C51E6-5-hIgG4/k-df-hIL-2 (T3A/D20A/R38E/C125A) HC hIL-2 in italics | QVQLVQSGSELKPKGASVKVSKASGYSLYGTSMHWVRQAPGGLEWVMGYISPFTRGRATYAQGFTGREV FSLDTSVSTAYLQISSLKAEDTAVYYCARDYDYYRYYYAMDYWGQGT TVTVSSASTKGPSVEPLAPCSRST TSESTAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSVTVPSSSLGKTKYTCNVDD HKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVLEFPKPKDTLMISRTPEVTCVVVDVSDPEVQF EPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVD KSRWQEGNVFSCVMHEALHNHYTQKLSLSLGLGKAPASSSTKKTQLQLEHLLALQMI LINGINNYKNPK <i>LTEMLTFKFKYMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLELKGSETTEM CEYADETATIVEFLNRWITFAQSIISTLT</i> |
| 551 | C51E6-5-hIgG4/k-LEPG-hIL-2 (T3A/D20A/R38E/C125A) HC hIL-2 in italics | QVQLVQSGSELKPKGASVKVSKASGYSLYGTSMHWVRQAPGGLEWVMGYISPFTRGRATYAQGFTGRFV FSLDTSVSTAYLQISSLKAEDTAVYYCARDYDYYRYYYAMDYWGQGT TVTVSSASTKGPSVEPLAPCSRST TSESTAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSVTVPSSSLGKTKYTCNVDD HKPSNTKVDKRVESKYGPPCPPCPAPEFEGGPSVLEFPKPKDTLMISRTPEVTCVVVDVSDPEVQF EPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVD KSRWQEGNVFSCVMHEALHNHYTQKLSLSLGLGKAPASSSTKKTQLQLEHLLALQMI LINGINNYKNPK <i>LTEMLTFKFKYMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLELKGSETTEM CEYADETATIVEFLNRWITFAQSIISTLT</i> |
| 552 | A2-hIgG4/k-LE HC | DVQLVESGGGLVQPGGSLRLSCAASGFTFDISAMSWVRQAPGKGLEWVSTISGSAYSTYYADSVKGRFT ISRDNKSTLYLQMNLSRAEDTAVYYCAREIFSDYWGLGLTVTVSSASTKGPSVEPLAPCSRSTSESTA ALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSVTVPSSSLGKTKYTCNVDDHKPSNT KVDKRVESKYGPPCPPCPAPEFEGGPSVLEFPKPKDTLMISRTPEVTCVVVDVSDPEVQFNWYVDG VEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVY LPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRWQ GNVFCSCVMHEALHNHYTQKLSLSLGLG |
| 553 | A2-hIgG4/k-LAGA HC | DVQLVESGGGLVQPGGSLRLSCAASGFTFDISAMSWVRQAPGKGLEWVSTISGSAYSTYYADSVKGRFT ISRDNKSTLYLQMNLSRAEDTAVYYCAREIFSDYWGLGLTVTVSSASTKGPSVFPPLAPCSRSTSESTA ALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSVTVPSSSLGKTKYTCNVDDHKPSNT KVDKRVESKYGPPCPPCPAPEFaGaPSVLEFPKPKDTLMISRTPEVTCVVVDVSDPEVQFNWYVDG VEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVY LPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRWQ GNVFCSCVMHEALHNHYTQKLSLSLGLG |
| 554 | A2-hIgG4/k-LEPG HC | DVQLVESGGGLVQPGGSLRLSCAASGFTFDISAMSWVRQAPGKGLEWVSTISGSAYSTYYADSVKGRFT ISRDNKSTLYLQMNLSRAEDTAVYYCAREIFSDYWGLGLTVTVSSASTKGPSVFPPLAPCSRSTSESTA ALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSVTVPSSSLGKTKYTCNVDDHKPSNT KVDKRVESKYGPPCPPCPAPEFEGGPSVLEFPKPKDTLMISRTPEVTCVVVDVSDPEVQFNWYVDG VEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLGSSIEKTI SKAKGQPREPQVY LPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRWQ GNVFCSCVMHEALHNHYTQKLSLSLGLG |
| 555 | A2-hIgG4/k-df-hIL-2 (T3A/D20A/R38E/C125A) HC hIL-2 in italics | DVQLVESGGGLVQPGGSLRLSCAASGFTFDISAMSWVRQAPGKGLEWVSTISGSAYSTYYADSVKGRFT ISRDNKSTLYLQMNLSRAEDTAVYYCAREIFSDYWGLGLTVTVSSASTKGPSVFPPLAPCSRSTSESTA ALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSVTVPSSSLGKTKYTCNVDDHKPSNT KVDKRVESKYGPPCPPCPAPEFLGGPSVLEFPKPKDTLMISRTPEVTCVVVDVSDPEVQFNWYVDG VEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVY LPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRWQ GNVFCSCVMHEALHNHYTQKLSLSLGLGKAPASSSTKKTQLQLEHLLALQMI LINGINNYKNPKL <i>TEMLTFKFKYMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLISNINVI VLELKGSETTEM CEYADETATIVEFLNRWITFAQSIISTLT</i> |

TABLE 29-continued

| Sequences | | |
|------------|---|---|
| SEQ ID NO: | Name | Sequence |
| 556 | A2-hIgG4/k-LE-df-hIL-2 (T3A/D20A/R38E/C125A) HC hIL-2 in <i>italics</i> | DVQLVESGGGLVQPGGSLRLSCAASGFTFDISAMSWVRQAPGKGLEWVSTISGSAYSTYYADSVKGRET ISRDNSKSTLYLQMNSLRAEDTAVYYCAREIFSDYWGGLTLVTVSSASTKGPSVFPPLAPCSRSTSESTA ALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNVDHKPSNT KVDKRVESKYGPPCPPCPAPEFEGGSPVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWYVDG VEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVY LPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRWQE GNVFCSCVMHEALHNHYTQKSLSLGLKAPASSSTKKTQLQLEHLLALQMI LINGINNYKNPKLTEM LTKFYPMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLISININVI VLELKGSETTEMCEYADE TATVEFLNRWITFAQSIISTLT |
| 557 | A2-hIgG4/k-LAGA-df-hIL-2 (T3A/D20A/R38E/C125A) HC hIL-2 in <i>italics</i> | DVQLVESGGGLVQPGGSLRLSCAASGFTFDISAMSWVRQAPGKGLEWVSTISGSAYSTYYADSVKGRET ISRDNSKSTLYLQMNSLRAEDTAVYYCAREIFSDYWGGLTLVTVSSASTKGPSVFPPLAPCSRSTSESTA ALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNVDHKPSNT KVDKRVESKYGPPCPPCPAPEFAGAPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWYVDG VEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVY LPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRWQE GNVFCSCVMHEALHNHYTQKSLSLGLKAPASSSTKKTQLQLEHLLALQMI LINGINNYKNPKLTEM LTKFYPMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLISININVI VLELKGSETTEMCEYADE TATVEFLNRWITFAQSIISTLT |
| 558 | A2-hIgG4/k-LEPG-df-hIL-2 (T3A/D20A/R38E/C125A) HC hIL-2 in <i>italics</i> | DVQLVESGGGLVQPGGSLRLSCAASGFTFDISAMSWVRQAPGKGLEWVSTISGSAYSTYYADSVKGRFT ISRDNSKSTLYLQMNSLRAEDTAVYYCAREIFSDYWGGLTLVTVSSASTKGPSVFPPLAPCSRSTSESTA ALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNVDHKPSNT KVDKRVESKYGPPCPPCPAPEFEGGSPVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWYVDG VEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLGSSIEKTI SKAKGQPREPQVY LPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRWQE GNVFCSCVMHEALHNHYTQKSLSLGLKAPASSSTKKTQLQLEHLLALQMI LINGINNYKNPKLTEM LTKFYPMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNEHLRPRDLISININVI VLELKGSETTEMCEYADE TATVEFLNRWITFAQSIISTLT |
| 559 | Anti-hPD-1 #1 HC | QVQLVESGGGVVQPGRSLRLDCKASGITFSNSGMHWVRQAPGKGLEWVAVIWDGSKRYADSVKGRFT ISRDNSKNTLFLQMNSLRAEDTAVYYCATNDYWGQGLTVTVSSASTKGPSVFPPLAPCSRSTSESTAAL GCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNVDHKPSNTKV DKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSDQEDPEVQFNWYVDGVE VHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVY LPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSRWQEGN VFCSCVMHEALHNHYTQKSLSLGLG |
| 560 | Anti-CD20-hIgG1/k HC | QVQLQQPGAELVKPGASVKMCKASGYTFTSYNMHWVKQTPGRGLEWIGAIYIPNGDTSYINQKEKGGKAT LTADKSSSTAYMQLSSLTSEDSAVYYCARSTYYGGDWYFNVWGAGTIVTVSAASTKGPSVFPPLAPSSKS TSGGTAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVN HKPSNTKVDKKEPKSCDKTHTCPPCPAPELGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPE VKFNWYVDGVEVHNAKTKPREEQYNSYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI SKAKG QPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKL TVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGK |
| 561 | Anti-CD20-hIgG1/k-LAGA HC | QVQLQQPGAELVKPGASVKMCKASGYTFTSYNMHWVKQTPGRGLEWIGAIYIPNGDTSYINQKEKGGKAT LTADKSSSTAYMQLSSLTSEDSAVYYCARSTYYGGDWYFNVWGAGTIVTVSAASTKGPSVFPPLAPSSKS TSGGTAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVN HKPSNTKVDKKEPKSCDKTHTCPPCPAPELAGAPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPE VKFNWYVDGVEVHNAKTKPREEQYNSYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI SKAKG QPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKL TVDKSRWQQGNVFCSCVMHEALHNHYTQKSLSLSPG |
| 562 | Anti-CD20-hKappa LC | QIVLSQSPAILSASPGEKVTMTCRASSSVSYIHWFPQQKPGSSPKPIYATSNLASGVPVRESGSGSGTS YSLTISRVEAEDAATYYCQQTWTSNPPTFGGGKLEIKRTVAAPSVPFIPPSDBQLKSGTASVCLLNE YPREAKVQNKVDNALQSGNSQESVTEQDSKDSYLSSTLTLSKADYKHKVYACEVTHQGLSSPVTKS ENRGE |
| 563 | 1H3-hIgG1-LAGA-df-hIL-2 (T3A/C125A) HC hIL-2 in <i>italics</i> | EVQLVESGGGLVQPGRSLKLSCAVSGFTESDYAMAWVRQAPKKGLEWVATISYDGSRTYYRDSVKGRFT ISRDNAKITLYLQMQSLRSEDATAYCARHSGSYFDYWGQGMVTVSSASTKGPSVFPPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHPKS NTKVDKKEPKSCDKTHTCPPCPAPELAGAPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEKVEN WYVDGVEVHNAKTKPREEQYNSYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI SKAKGQPRE PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDK SRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGKAPASSSTKKTQLQLEHLLDLQMI LINGINNYKNPKL TRMLTKFYPMPKKA TELKHLQCLEEELKPLEEVLNLAQSKNFHLRPRDLISININVI VLELKGSETTEM CEYADETATVEFLNRWITFAQSIISTLT |

TABLE 29-continued

| Sequences | | |
|-----------|--|---|
| SEQ ID | Name | Sequence |
| 564 | anti-mPD-1 RMP1-14 mIgG2b-N297A HC | EVQLQESGPGLVKPSQSLSTCSVTGYSITSSYRWNRWIRKFPNGRLEWMGYINSAGISNYNPSLKRRIS ITRDTSKNQFFLQVNSVTTEDAATYYCARSDNMGTPFTYWGQGLVTVSSAKTTPPSVYPLAPGCGDT TGSSVTLGCLVKGYFPESVTVTWNSGSLSSVHTFPALLQSGLYTMSSSVTVPSSTWPSQTVTCSVAHP ASSTTVDKKLEPSGPISTINPCPPCKECKCPAPNLEGGPSVFI FPPNIKDVLMI SLTPKVT CVVVDVS EDDPDVQISWVFNNEVHTAQTQTHREDYASTIRVVSTLPIQHODWMSGKEFKCKVNNKDLPSPIERTI SKI KGLVRAPQVYILPPPAEQLSRKDVSLTCLVVGGENPGDISVEWTSNGHTEENYKDTAPVLDSDGSYF IYSKLNMKTSKWEKTD SFCNVRHEGLKNYYLKKTI SRSPGK |
| 565 | anti-mPD-1 RMP1-14 mIgG2b-N297A- L6-hIL-2 (F42K/Y45R/ V69R) HC linker in dashed underline hIL-2 in italics | EVQLQESGPGLVKPSQSLSTCSVTGYSITSSYRWNRWIRKFPNGRLEWMGYINSAGISNYNPSLKRRIS ITRDTSKNQFFLQVNSVTTEDAATYYCARSDNMGTPFTYWGQGLVTVSSAKTTPPSVYPLAPGCGDT TGSSVTLGCLVKGYFPESVTVTWNSGSLSSVHTFPALLQSGLYTMSSSVTVPSSTWPSQTVTCSVAHP ASSTTVDKKLEPSGPISTINPCPPCKECKCPAPNLEGGPSVFI FPPNIKDVLMI SLTPKVT CVVVDVS EDDPDVQISWVFNNEVHTAQTQTHREDYASTIRVVSTLPIQHODWMSGKEFKCKVNNKDLPSPIERTI SKI KGLVRAPQVYILPPPAEQLSRKDVSLTCLVVGGENPGDISVEWTSNGHTEENYKDTAPVLDSDGSYF SRWQQGNVFS CSMHEALHNNHYTQKLSLSLSPGKSGGGGSA PAS SSTKKTQLQLEHLLALQMILNGINN QMILNGINNYKNPKLTRMLTKKERMPPKATELKHLCLEELKPLEERLNLQAQSKNFHLRPRDLISNIN VIVLELKGSETTEMCEYADETATIVEFLNRWITFCQSIISTLT |
| 566 | anti-mPD-1 RMP1-14 mKappa LC | DIVMTQGTLPNPVPSGESVSIITCRSSKSLLYSDGKTYLNWYLQRPQSPQLLIYWMSTRASGVSDRESG SGSGDFTLKI SGVEAEDVGIYYCQQGLEFPFTFGGGTKLELKRADAAPT VSI FPPSSEQLTSGGASVVC FLMNFYPKDINVKWKIDGSRQNGVLNSWTDQSDKSTYSMSSTLTLTKDEYERHNSYTCEATHKTST PIVKS ENRNEC |
| 567 | anti-mPD-1 RMP1-30 mIgG2b-N297A HC | EVQLVESGGGLVQPGRSRLKLSAASGFTFGDY SMAWVRQAPKRGLEWVANIIYDGSRTFYRDSVKGRFT ISRDNAKPTLYLQMDSLRPEDTATYYCATHNYPGYAMEAWGQGT SVTVSSAKTTPPSVYPLAPGCGDTT GSSVTLGCLVKGYFPESVTVTWNSGSLSSVHTFPALLQSGLYTMSSSVTVPSSTWPSQTVTCSVAHPA SSTTVDKKLEPSGPISTINPCPPCKECKCPAPNLEGGPSVFI FPPNIKDVLMI SLTPKVT CVVVDVSE DDPDVQISWVFNNEVHTAQTQTHREDYASTIRVVSTLPIQHODWMSGKEFKCKVNNKDLPSPIERTIS KI KGLVRAPQVYILPPPAEQLSRKDVSLTCLVVGGENPGDISVEWTSNGHTEENYKDTAPVLDSDGSYFI YSKLNMKTSKWEKTD SFCNVRHEGLKNYYLKKTI SRSPGK |
| 568 | anti-mPD-1 RMP1-30 mKappa LC | DTVLTQSPALPVSLGQRVNI SCRATKSVSRVYVHWYQQKSGQQPRLLIYTTSNLESGVPSRFSGGSGGSDT FLLTIDPVEADDIANYCQQSNEI PYTFGAGTKLELKRADAAPT VSI FPPSSEQLTSGGASVVC YPKDINVKWKIDGSRQNGVLNSWTDQSDKSTYSMSSTLTLTKDEYERHNSYTCEATHKTST PIVKS ENRNEC |
| 569 | anti-mPD-1 RMP1-30 mIgG2b-N297A- L6-hIL-2 (F42K/Y45R/ V69R) HC linker in dashed underline hIL-2 in italics | EVQLVESGGGLVQPGRSRLKLSAASGFTFGDY SMAWVRQAPKRGLEWVANIIYDGSRTFYRDSVKGRFT ISRDNAKPTLYLQMDSLRPEDTATYYCATHNYPGYAMEAWGQGT SVTVSSAKTTPPSVYPLAPGCGDTT GSSVTLGCLVKGYFPESVTVTWNSGSLSSVHTFPALLQSGLYTMSSSVTVPSSTWPSQTVTCSVAHPA SSTTVDKKLEPSGPISTINPCPPCKECKCPAPNLEGGPSVFI FPPNIKDVLMI SLTPKVT CVVVDVSE DDPDVQISWVFNNEVHTAQTQTHREDYASTIRVVSTLPIQHODWMSGKEFKCKVNNKDLPSPIERTIS KI KGLVRAPQVYILPPPAEQLSRKDVSLTCLVVGGENPGDISVEWTSNGHTEENYKDTAPVLDSDGSYF IYSKLNMKTSKWEKTD SFCNVRHEGLKNYYLKKTI SRSPGKSGGGGSA P TSSSTKKTQLQLEHLLLDL MILNGINNYKNPKLTRMLTKKFrMPKKATELKHLCLEELKPLEERLNLQAQSKNFHLRPRDLISNIN VIVLELKGSETTEMCEYADETATIVEFLNRWITFCQSIISTLT |
| 570 | anti-KLH-C3- mIgG2b-N297A- L6-hIL-2 (F42K/Y45R/ V69R) HC linker in dashed underline hIL-2 in italics | EVQLVSGGGGLVQPGGSLKLSAASGFTFSDFYMAWVRQAPTKGLEWVASISTGGGNTHYRDSVKGRFT ISRDNAKSTLYLQMDSLRSEETATYYCARLLSTISTPFDYWGQGVIVTVSSAKTTPPSVYPLAPGCGDT TGSSVTLGCLVKGYFPESVTVTWNSGSLSSVHTFPALLQSGLYTMSSSVTVPSSTWPSQTVTCSVAHP ASSTTVDKKLEPSGPISTINPCPPCKECKCPAPNLEGGPSVFI FPPNIKDVLMI SLTPKVT CVVVDVS EDDPDVQISWVFNNEVHTAQTQTHREDYASTIRVVSTLPIQHODWMSGKEFKCKVNNKDLPSPIERTI SKI KGLVRAPQVYILPPPAEQLSRKDVSLTCLVVGGENPGDISVEWTSNGHTEENYKDTAPVLDSDGSYF IYSKLNMKTSKWEKTD SFCNVRHEGLKNYYLKKTI SRSPGKSGGGGSA P TSSSTKKTQLQLEHLLLDL QMILNGINNYKNPKLTRMLTKKFrMPKKATELKHLCLEELKPLEERLNLQAQSKNFHLRPRDLISNIN VIVLELKGSETTEMCEYADETATIVEFLNRWITFCQSIISTLT |
| 571 | KLH-C3-mKappa LC | DVVLIQSPTTSLVTPGETVLS CRASHSVGTNLHWYQQR TNESPSLLIKYSSHSTSGIPSRSATSGST DFTLNI SNVEFDDVASYFCQQSQKWLTPFGSGTKLEIKRADAAPT VSI FPPSSEQLTSGGASVVC FYPKDINVKWKIDGSRQNGVLNSWTDQSDKSTYSMSSTLTLTKDEYERHNSYTCEATHKTST PIVKS ENRNEC |

TABLE 29-continued

| Sequences | | |
|------------|--|--|
| SEQ ID NO: | Name | Sequence |
| 572 | 2D12-hIgG1-L6-hIL-2 HC linker in dashed underline hIL-2 in italics | EVQLQQSGPELVKPGASVKISCKTSGYTFTEYTMHWVKQSHGKSLLEWIGGINPNNGGTTYNQKFKGKAT LTVDKSSSTAYMELRSLTSQDSAVYYCARDYRIGHYIYAMDYWGQTSVTVSSASTKGPSVFPPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTQTYICNV NHKPSNTKVDKRVESKYGPPCPPAPEFLGGPSVLEFPPKPKDTLMI SRTPEVTCVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI SKAK GQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSK YSKLNMTSKWEKTDSPFCNVRHEGLKNVYLKKTISRSPGKSGGGGSAPTSSSTKKTQLQLEHLLLDLQ NGINNYKNPKLTRMLTFKPYMPKKATELKHLCLEELKPLEEVLNLAQSKNFHLRPRDLISNINVIVL ELKGETTEMCEYADETATIVEFLNRWITFCQSIISTLT |
| 573 | 2D12-hKappa LC | QIVLTQSPAIMASAPGEKVTMTCSVSSSREMHWYQQKSGTSPKRWIYDTSKLASGVPARFSGSGSGTS YSLTISSMEADAATYCCQQWSNPPTFGGGTKLKIKRRTVAAPSVFIFPPSDEQLKSGTASVCLLNNE YPREAKVQWKVDNALQSGNSQESVTEQDSKDSSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKS FNRGEC |
| 574 | hIL-2 F42A/Y45A/L72G | APTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTAKFAMPKKATELKHLCLEELKPLEEV LNGAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSIISTLT |
| 575 | hIL-2 H16A/F42A | APTSSSTKKTQLQLEALLLDLQMI LNGINNYKNPKLTRMLTAKFAMPKKATELKHLCLEELKPLEEV LNLAQSKNFHLRPRDLISNINVIVLELKGSETTEMCEYADETATIVEFLNRWITFCQSIISTLT |
| 576 | 1H9-hIgG4 HC | EVQLLESGGGLVQPGGSLRLSCVGSFENLKYCMTWVRQAPGKGLEWVSAIVYSGGSTYIADSVKGRFT ISRDNKNTLYLQMNSLRAEDTAVYYCAKYTRGSYFYDAMDVWGQTTVTVSSASTKGPSVFPPLAPCSR STSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTQTYICNV DHKPSNTKVDKRVESKYGPPCPPAPEFLGGPSVLEFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVQ FNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQP REPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTV DKSRWQEGNVFSCVMHEALHNHYTQKSLSLSLG |
| 577 | 1D5-hIgG4 HC | EVQLLESGGGLVQPGGSLRLSCVGSFENLKYCMTWVRQAPGKGLEWVSAIVYSGGSTYIADSVKGRFT ISRDNKNTLYLQMNSLRAEDTAVYYCAKYTRGSYFYDAMDVWGQTTVTVSSASTKGPSVFPPLAPCSR STSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTQTYICNV DHKPSNTKVDKRVESKYGPPCPPAPEFLGGPSVLEFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVQ FNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQP REPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTV DKSRWQEGNVFSCVMHEALHNHYTQKSLSLSLG |
| 578 | Anti-hPD-1 #2 HC | QVQLVQSGVEVKKPGASVKVSKASGYTFPTNYMYWVRQAPGQGLEWMGGINPNSGGTNFNEKFKNRVT LITDSSSTTAYMELKSLQPDVTAVYYCARRDYRFDMGDFYWGQTTVTVSSASTKGPSVFPPLAPCSRST SESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTQTYICNV KPSNTKVDKRVESKYGPPCPPAPEFLGGPSVLEFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVFN WYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPRE PQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTV DKSRWQEGNVFSCVMHEALHNHYTQKSLSLSLG |
| 579 | Anti-hPD-1 #2 LC | EIVLTQSPATLSLSPGERATLSCRASKGVSTSGYSYLHWYQQKPGQAPRLLIYLAAYLESGLVQPARFSGS GSGTDFLTITISLEPEDFAVYYCQHSRDLPLTFGGGTKVEIKRRTVAAPSVFIFPPSDEQLKSGTASVVC LINFYYPREAKVQWKVDNALQSGNSQESVTEQDSKDSSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSS PVTKSENREGEC |
| 580 | human PD-1 receptor lentiviral vector | gtcgacggatcgaggagatctccgatccccataggtgcaactctcagtacaatctgctctgatgccgcat agttaagccagatctgctccccctgctgtgtgtggaggtcgctcagtagtgccgagcaaaaatttaag ctacaacaaggcaaggcttgaccgacaatgcatgaagaatctgcttagggttaggcgttttgccgtgc ttcgcgatgtacgggagatatacgcgttgacatgatatgactagttattaatagtaatacaat cggggctcatagttcatagcccatatagggagttccgctgacataactacgggtaaatggccccctg gctgacgccccaacgacccccgcccattgacgtcaataatgacgtatgctcccatagtaaacgcaatag ggactttccatgacgtcaatggggtggagatttaacggtaaacctgcccactggcagtaacatcaaggt atcatatgccaagtacgccccctattgacgtcaatgacggtaaatggccccctgagcatatgcccag acatgaccttagggactttcctactggcagtagctcactcgtattagctcagctattacacaggtga tgcggttttgccagtagctcaatgggctggatagcggtttgactcaggggatttccaagctccacc ccattgacgtcaatgggagttgtttggcaccaaaatacaacgggactttccaaaatgctcgtaacaa ccgccccatgacgcaaatgggctggtagcgtgtaacgggtggaggtctatataagcagcgcgtttg tgtactgggtctctctggttagacagatctgagcctgggagctctctggctaacctagggaaacccatg cttaagcctcaataagcttgccctgagtgctcaagtagtggtgctgctgctgctgctgctgctgctg aactagagatccctcagacccttttagttagtggaatactcagcagtgggcccgaaacgggact tgaaagcgaaggaaacagaggagctctctcagcagaggactcggcttgctgaaagcgcgcaacggc gagggcagggggcggcagctggtgagtagcggcaaaaatttgactagcggaggctagaaggagagatg gggtgcgagagcgtcagtagtaagcgggggagaatagatcgcgtaggggaaatactcgtttaaagccag ggggaagaaaaaataaataaaaacatagtagggcaagcagggagctagaacgattcgcagctta atcctggcctgtagaaacatcagaaggcttagacaaatactgggacagctacaacatccccatcaga cagtagcagaagaacttagatcatatataacagtagcaaccctctatgtgtgcatcaagagtag agataaaagacccaaggagctttagacaagatagaggaagagcaaaaacaaaagtaagaccaccgac agcaagcggccgctgactctcagacctggaggaggagatagagggacaattggagaagtgaattat |

TABLE 29-continued

| Sequences | | |
|--------------------|--|--|
| SEQ ID NO: Name | Sequence | |
| | aaatataaagt agt aaaaa tgaaccatt aggagtagc acccacc aaggcaagaga agagt ggt gcag agagaaaaa agcagtg ggaat aggagct t t gtt cct tgggt tct tgggagc agcagga agcact at g ggccagcgt caatgacgt gacggtagc agccagaca at t atgt ct ggt at agt g cagc agcagaac aat t t gct gagggt at t gaggc gcaac agc at ct gt t gca act cac agt ct ggggc at caagc agct c caggcaaga at cctggct gt ggaagat acc t aaaggat caacagct cctgggt t tgggggt t gct ct ggaaact cat t tgcacc act gct gt gct tggaa t gct agt tggagt aataat ct ct ggaacagat t tggaa t cacacgacct ggt agt gggacagaga aat t acaat t acaca agct t aat acact cct a at t gaa gaat c gcaaa acc agca a gaa a ga at gaaca ga at t t gga at tagat aat g gga a agt t t g t g g a a t t g g t t a a c a t a c a a a t t g g c t g t g g t a t a t a a a t t a t t c a t a a t g a t a g t a g g a g g c t t g g t a g g t t t a a g a a t a g t t t t g c t g t a c t t c t a t a g t g a a t a g a g t a g g c a g g g a t a t c a c c a t t a t c g t t c a g a c c c a c c t c c c a c c c c g a g g g g a c c c g a c a g g c c c g a a g g a a t a g a a g a a g g t g g a g a g a g a c a g a g a c a g a t c c a t t c g a t a g t g a a c g g a t c g g c a c t g c g t g c c c a a t t c t g c a g a c a a a t g g c a g t a t t c a t c c a c a a t t t t a a a g a a a a g g g g g g a t t g g g g g t a c a g t g c a g g g g a a a g a a t a g t a g a c a t a a t a g c a a c a g a c a t a c a a a c t a a a g a a t t a c a a a a c a a a t t a c a a a a t t c a a a a t t t c g g g t t a t a c a g g g a c a g c a g a g a t c c a g t t t g g t a a t a a g t a a t c g c t a g c t a g g t c t t g a a g g a g t g g g a a t t g g c t c c g g t g c c c g t c a g t g g g c a g a g c c a c a t c g c c c a c a g t c c c c g a g a t t g g g g g a g g g g t c g g c a a t t g a t c c g g t g c c t a g a g a g g t g g c g c g g g g t a a a c t g g g a a g t g a t g t c g t g a c t g g c t c c g c c t t t t c c c a g g g t g g g g a g a a c c g t a t a a a g t g c a g t a g t c g c c g t g a a c g t t c t t t t c g c a a c g g g t t g c c g c c a g a a c a c a g g a c c g g t t c t a g a g c g t g c c a c c a t g c a g a t c c c a c a g g c g c c c t g g c c a g t c g t c t g g c g g t g c t a c a a c t g g g c t g g c g g c c a g g a t g c t t a g a c t c c c a g a c a g g c c t g g a a c c c c c a c c t t c t c c c a g c c c t g c t g t g g t g a c c g a a g g g g a c a a c g c c a c c t t c a c c t g c a g t t c t c c a a c a c a t c g g a g a g c t c g t g c t a a a c t g g t a c c g c a t g a g c c c a g c a a c c a g a c g g a c a a g c t g g c g c c t c c c c a g g a c c g c a g c c a g c c c g g c c a g g a t c c g c t t c c g t g t c a c a c a a c t g c c a a c g g g c g t g a c t t c c a c a t g a g c g t g g t c a g g g c c g g c g c a a t g a c a g c g g c a c c t a c c t c t g t g g g g c a t c t c c t g g c c c c a a g g c g c a g a t c a a a g a g a g c t g c g g g c a g a g c t c a g g g t g a c a g a g a g a a g g g c a g a a g t g c c c a c a g c c c a c c c a g c c c c t c a c c a a g g c c a g c c g g c c a g t t c a a a c c c t g g t g g t t g g t g t c g t g g g c g g c t g c t g g g c a g c c t g g t g c t g t a g t c t g g g t c c t g g c c g t c a t c t g c t c c c g g g c c g c a g a g g g a c a a t a g g a g c a g g c g c a c c g g c a g c c c t g a a g g a g g a c c c c t c a g c c g t g c c t g t g t t c t c t g t g g a c t a t g g g g a g c t g g a t t t c a g t g g c g a g a g a a g a c c c g g a g c c c c c g t g c c t g t g t c c c t g a g c a g a c g g a g t a t g c c a c c a t t g t c t t c t c a g c g g a a t g g g c a c c t c a t c c c c c g c c c g c a g g g g c t c a g t g a c g g c c c t c g g a g t g c c a g c c a c t g a g c c t g a g g a t g g a c a c t g c t c t t g g c c c c t c t g a g c c c c t c c c t c c c c c c c c t a a c g t t a c g t t a c t g g c g a a g c g c t t g g a a t a a g g c c g t g t g c g t t t g t c t a t a g t t a t t t c c a c c a t a t g c c g t c t t t g c c a a a g g a a t g c a a g g t c t g t g a a t g t c g t g a a g g a a g c a g t t c c t c t g g a a g t t c t t g a a g a c a a a c a a c g t c t g t a g c g a c c c t t g c a g g c a g c g g a a c c c c a c c t g g c g a c a g g t g c c t c t g c g g c c a a a a g c c a c g t g t a t a a g a t a c a c t g c a a a g g c g g c a c a c c c a g t g c c a c g t g t g a g t t g g a t a g t t g t g g a a a g a g t c a a t a a g g t c t c c t c a a g c g t a t t c a a c a a g g g g t g a a g g a t g c c a g a a c c c c a t t g t a t g g g a t c t g a t c t g g g g c c t c g t g c a c a t g c t t a c a t g t g t t a g t c g a g g t t a a a a a a a c g t c t a g g c c c c c g a a c c a c g g g a c g t g g t t t c c t t g a a a a a c a c a g a t g a t a a t a t g g c c a a a t g a c c a g t a c a a g c c c a c g g t g c g c c t c g c c a c c c g c g a c a g c t c c c a g g g c c g t a c g c a c c c t c g c g c c g c g t t c g c c g a c t a c c c c g c c a c g c c a c a c c g t c g a t c c g g a c c g c a c a t c g a g c g g g t a c c g a g c t g c a a g a a c t c t t c c t c a c g c g c t c g g g t c g a c a t c g g c a a g g t g t g g g t c g c g g a c a c g c g g g c c g c g g t g g c g g t c t g g c a c g c c g g a g a g c g t c g a a g c g g g g c g g t g t c g c c g a g a t c g g c c g c g c a t g g c c g a g t t g a g c g g t t c c c g g c t g g c c g c a g c a a c a g a t g g a a g g c c t c c t g g c g c g c a c c g g c c a a g g a g c c c g c g t g g t t c c t g g c a c c g t c g g a g t c t g c c c g a c c a c a g g g c a a g g g t c t g g c a g c g c g t c g t g c t c c c c g g a g t g g a g g c g g c g a g c g c g c c g g g t g c c c g c c t c t c t g g a g c t c c g c g c c c g c a a c c t c c c t t c t a c a g a c g g c t c g g t t c a c c g t c a c c g c c a c g t c g a g g t g c c g a a g g a c c g c a c c t g g t g c a t g a c c g c a a g c c g g t g c t g a a c g c g t a a g t c g a c a a t a a c c t c t g g a t t a c a a a a t t g t g a a a g a t t g a c t g g t a t t c t t a a c t a t g t t g c t c c t t t a c g t t a t g g a t a c g c t g c t t a a t g c c t t g t a t c a t g c t a t t g c t c c c g t a t g g c t t c a t t t t c t c c t c c t g t a t a a t c c t g g t t g c t g t c t t t a t g a g g a g t t g t g g c c g t g t c a g g c a a c g t g g c g t g g t g t g c a c t t g t t t g c t g a c g e a a c c c c a c t g g t t g g g c a t t g c c a c c a c c t g t c a g c t c c t t c c g g g a c t t c g c t t c c c c t c c c t a t t g c c a c g g c g g a a c t c a t c g c c g c t g c c t t g c c g c t g c t g g a c a g g g g c t c g g c t g t g g g c a c t g a c a a t c c g t g g t g t g t c g g g g a a a t c a t c g t c c t t c c t t g g c t g c t c g c t g t g t g c c a c c t g g a t t c t g c g c g g g a c g t c c t t c t g c t a c g t c c c t c g g c c c t a a t c a a g c g g a c c t t c c t c c c g c g g c t g t g c c g g c t c t g c g g c c t t c c g c g t c t c g c c t c g c c c t a g a c a g a g t c g g a t c t c c c t t g g g c g c c t c c c g c g t c g a c t t a a g a c c a a t g a c t t a c a a g g c a g c t g t a g a t t a g c a c t t t t a a a g a a a a g g g g g a c t g g a a g g g c a a t t c a c t c c c a a c g a a g a c a a c a c t c g c t t t t g c t g t a c t g g g t c t c t c g g t t a g a c c a g a t c t g a g c c t g g g a g c t c t c t g g c t a a c t a g g g a a c c c a c t g c t t a a g c c t a a t a a a g c t t g c c t t g a g t g c t c a a g t a g t g t g t g c c c g t c t g t g t g t a c t c t g g t a a c t a g a g a t c c c t c a g a c c c t t t a g t c a g t g t g g a a a t c t c t a g c a g g g c c g t t a a a c c c g c t g a t a g c c t c g a c t g t g c c t t c t a g t g c c a g c c a t c t g t t g t t g c c c c t c c c c g t g c c t t c c t t g a c c c t g g a a g g t g c c a c t c c c a c t g t c c t t c c t a a t a a a a t a a g g a a a t g c a t c g c a t t g t c t g a t a g g t g c a t t c t a t c t g g g g g t g g g g t g g g c a g g a c a g c a a g g g g g a g g a t t g g g a a g a c a a t a g c a g g c a t g c t g g g g a t g c g g t g g g c t c a t g g c t c t g a g g c g g a a a g a a c c a g c t g g g c t c t a g g g g g t a t c c c a c g c g c c t g t a g c g g c a t t a a g c g c g c g g g t g t g g t g g t a c g c g c a g c g t g a c c g t a c a c t t g c c a g c c c t a g c g c c c g c c c t t t e g t t t c t c c c t c c t t c t c g c g a c t t c g c c g g c t t c c c c g t c a a g c t c a a a t c g g g g g c c c c t t a g g g t t c c g a t t a g t g c t t a c g g c a c c t c g a c c c a a a a a a a a c t t g a t t a g g g t g a t g g t t c a c g t a g t g g g c a t c g c c c t g a t a g a c g g t t t t c g c c c t t g a c g t g g a g t c c a c g t t c t t a a t a g t g g a c t c t g t t c c a a a c t g g a a c a a c a c t c a a c c c t a t c t c g g t c t a t t c t t t g a t t a a a g g g a t t t g c c g a t t c g g c c t a t t g g t t a a a a a t g a g c t g a t t a a c a a a a a t t a a c g c g a a t a a t t c t g t g g a a t g t g t c a g t t a g g g t g t g g a a a g t c c c a g g t c c c c a g c a g g c a g a a g t a t g c a a a g c a t g c a t c a a t a g t c a g c a a c c a g g t g t g g a a a g t c c c a g g c t c c c a g c a g g c a g a a g t a t g c a a a g c a t g c a t c a a t a g t c a g c a a c c a g g t g t g g a a a g t | |

TABLE 29-continued

| Sequences | | |
|-----------|---|--|
| SEQ ID | Name | Sequence |
| | | ccctaactcggccatccccccctaactcggccagttcggccatttccgccccatgggtgactaa ttttttttatgatgcagagccgagggcgcctctgcctctgagctattccagaagtgtgagaggct ttttggaggcctaggctttgcaaaaagctcccgggagctgtatccatttcggatctgatcagc acgtgttgacaataatcatcggcatagtatacggcatagtataacagcaaaagtgaggaaactaaac catggccaagtgtaccagtgccgttccgggtgctcaccgcgccgagctcggcgagcggctcgtctc gaccgaccggctcgggttctcccgggactcgtggaggacgactcggcgggtggtcgggacgagct gaccctgttcatcagcgggtccaggaccaggtggtgcccggacaacacctggcctgggtgtgggtg cggcctggacgagctgtacggcagtggtcggaggtcgtgtccacgaactcgggagcgcctcggggc ggccatgacogagatcggcgagcagcgtgggggggggagttcgccctcggcgaccggccggcaactg cgtgcactcgtggcggagagcaggactgacacgtgctacgagatctcgatccaccggccctctca tgaagggtgggcttcggaactcgtttccgggacggcggctggatgatctccagcggggatcagat gctggagttctcggccaccccaacttgtttatgacagcttataatggttacaataaagcaatagcat cacaaatccacaataaagcattttttcactgcattctagttgtggtttgtccaaactcaatgat atcttcatgctctgtataccgtcgacctctagctagagcttggcgtaatacaggtcatagctgttcc tgtgtgaaatgttatccgctcacaatccacacaacatcagagccggaagcataaagtgtaaagcctg gggtgctaatgagtgagctaaactcacatataatgctgtgctcactgcccgttccagtcgggaaa cgtcgtgccagctgcatataatgaaatcggccaacggcggggagaggcgggtttgctgtatggggc ttccgcttccctcgtcactgactcgtgctcgtcgtcggctcggcgagcgggtatcagctcactc aaaggcggtaaatcgggtatccacagaatcaggggataacgcaggaaagaacatgtgagcaaaaaggca gaaaaggccaggaaccgtaaaaaggccgcttggcggcgttttccataggctccgccccctgacga gcatcaaaaaatcgacgctcaagtacagaggtggcgaacccgacaggactataaagataccaggcgtt tccccctggaagctcctcgtgctcctcgttccgaccctcggccttaccggataccctgctccgctt ctccctcgggaagcgtggcgttctcactagctcagctgtaggtatctcagttcgggtgaggtcgt tcgctccaagctgggctgtgtgacgaaccccccttcagcccgaccgctcggccttatccggtaacta tcgtcttgagtcacaacccggtaagacacgactatcgccactggcagcagccactggtaacaggatgag cagagcagaggtatgtaggcgtgctacagagttctgaaagtggtggcctaaactaccggctacactagaag aacagttatgtgtatctgctcgtgtaagccagttacctcggaaaaagagttggtagctcttgatc cggcaaaaaaacaccgctggtagcgggtgtttttgtttgcaagcagcagattacggcgagaaaaaa aggatctcaagaagatccttgatctttctacgggggtcagcagctcagtggaacgaaaaactca agggatttggtcatgagatatacaaaaaggatctcactagatcctttaaatataaaatgaagttt taaatcaatctaaagtataataggtaaacttggtctgacagttaccaatgcttaacagtgaggcacc tatctcagcgatctgctctatctgcttcatccatagttgctgactccccgctgctgataactacgact acgggagggcttaccatctggccccagtgctgcaatgataccgagagaccacgctcaccggctccaga tttatcagcaataaacagccagccggaagggcagcagcagaagtggtcctgcaacttatccgctc catccagctcattaatgttgcgggaagctagagtaagtagttcggccagttaatagttgcgcaactg tgtgcatctgctacagggcatcgtggtgtcacgctcgtcgtttggtatggctcattcagctcgggtc caacagatcaaggcgagttacatgatcccccatgtgtgcaaaaaagcgggttagctcctcgggtcctcc gactgtgacagaagtgaagtgcccgagctgttatcactcaggttatggcagcactgcaataatctct tactgtcatgcatccgtgaagtgctttctgctgactggtgagctcaaccgaagtcattctgagaata tgttatgcccggcagcaggttgctcttgcggcggcgtcaatcgggatataaccggccacatagcagaac tttaaaagtgctcatcattggaacacgcttctcggggcgaaaactctcaaggatcttaccgctgtgag atccagttcagatgtaaccactcgtgcaaccccaactgatctcagcatctttactttaccagcgtttc tgggtgagcaaaaaacaggaaggcaaaatgcccgaaaaaagggataaagggcgacacggaaatgtgaa actcatactctccttttcaatattatgaaagcattatcagggttatgtctcatgagcggatcact atttgaaatgatttagaaaaataaacaaatagggggtccggcgacattccccgaaaagtggccacctga c |
| 581 | hIL-2 V69R | APTSSSTKKKQLQLLEHLLLDLQMLNLNGINNYKPKLTRMLTFKPYMPKKATELKHLCLEELKPLEER LNLAQSKNFHLRPRDLISNINVIVLELKGSETTEMCEYADETATIVEFLNRWITFCQSIISTLT |
| 582 | H7-02-hIgG1- LAGA-df-hIL-2 (T3A/D20A/R38E/ C125A) HC | EVQLLESGGGLVQPGGSLRLSCAASGFTFKSYAMTWVRQAPGKLEWVSAIVYSGGSTYYADSVKGRFT ISRDNKNTLYLQMQNSLRADTAVYYCAKYTRASYFYDAMDVWGQTTVTVSSASTKGPSVFPPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNV NHKPSNTKVDKKEPKSCDKTHTCPPCPAPELAGAPSVLEFPKPKDTLMIKSRTEVTVVVDVSHEDP EVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIKAK GQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFPLYSK LTVDKSRWQOGNVPFSCVMHEALHNYTQKSLSLSPGKAPASSSTKTKQLQLLEHLLALQMLNLNGINNY KPKLTEMLETFKPYMPKKATELKHLCLEELKPLEEVLNLAQSKNFHLRPRDLISNINVIVLELKGSE TTFMCEYADETATIVEFLNRWITFAQSIISTLT |
| 583 | H7-02-hKappa LC | EIVLTQSPGTLISLSPGERATLSCRASQSISSSFLAWYQQKPGQAPRLLIYDASTRATGIPDRESGSGG TDFTLTISRLEPEDFAVYYCQQYDWPPLSFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVCLL NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSYSLSSLTLSKADYEKHKVYACEVTHQGLSSPV TKSENRC |
| 584 | hPD-L1 | MRIFAVEIFMTYWHLLNAFTVTPKDLVYVEYGSNMTIECKFPVEKQLDLAALIVWEMEDKNIIQFVH GEEDLVQHSYRQRARLLKQDLSLGNALQITDVKLQDAGVYRCMISYGGADYKRIIVKVNAPYKIN QRILVDPVTSHEELTCQAEYKPAEVIWTS SDHQVLSGKTTTNSKREKLEENVTSILRINTYNEIE YCTFRRLDPEENHTAELVIEPELPLAHPNERTHLVILGAILLCLGVALTFIERLRKGRMMDVKKCGIQD TNSKKQSDTHLEET |
| 585 | KLH-C3-hIgG4 HC | EVQLVSGGGGLVQPGGSIKLSAASGFTFSDFYMAWVRQAPTKGLEWVASISTGGGNTHYRDSVKGRFT ISRDNASTLYLQMQNSLRSEETATYYCARLISTISTPFDYWGQVIVTVSSASTKGPSVEPLAPCSRST SESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSIGTKTYTCDVH KPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVLEFPKPKDTLMIKSRTEVTVVVDVSDQEDPEVQEN |

TABLE 29-continued

| Sequences | | |
|------------|---|--|
| SEQ ID NO: | Name | Sequence |
| | | WYVDGVEVHNAKTKPREEQENSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTIISKAKGQPRE PQVYITPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRLTVDK SRWQEGNVESCSVMHEALHNNHYTQKLSLSLGLK |
| 586 | KLH-C3-hKappa LC | DVVLIIQSPTTSLVTPGETVSLSCRASHSVGTNLHWYQQRNESPILLIKYSSHSTSGIPSRFSATSGGT DETINISNVEFDDVASYFCQQSQKWLPTPGSGTKLEIKRVAAPSVEIFPPSDEQLKSGTASVVCLINN FYPREAKVQWKVDNALQSGNSQESVTEQDSKDSYSLSSLTLSKADYEKHKVYACEVTHQGLSSPVTK SENRRGEK |
| 587 | 1H3-hIgG1-L6- hCD25 (1-164)- L20-hIL-2 (E15A) HC | EVQLVESGGGLVQPGRSLKLSCAVSGETESDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGRET ISRDNAKITLYLQMDSLRSEDATYYCARHGSGYFDYWGQGMVTVSSASTKGPSVEPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSIIGTQTYICNVNHKPS NTKVDKKEVEPKSCDKTHTCPPCPAPELGGPSVFLFPPKPKDTLMI SRTPTEVTCVVVDVSHEDPEVKEN WYVDGVEVHNAKTKPREEQYNSYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPRE PQVYITLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDK SRWQQGNVSCSVMHEALHNNHYTQKLSLSLSPGKSGGGSELCDDDDPPEIPHATFKAMAYKEGTMLNCEC KRGFRRIKSGSLYMLCTGNSHSSWDNQCQCTSSATRNTTKQVTPQPEEQKERKTEMQSPMQPVDQAS LPGHCREPPPWENEATERIYHFVVGQMVYQCVQGYRALHRGPAESVCKMTHGKTRWTPQLICTSGGG GSGGGSGGGSGGGSAPTSSTTKTQLQLEHLLLDLQMLNGINNYKPNKLTTRMLTFKPYMPKKATEL KHLQCLEEELKPLEEVINLAQSKNPHLRPRDLISNINVI VLELKGSETTFMCEYADETATIVFELNRWI TFCQSIISTLT |
| 588 | 1H3-hIgG1-L6- hCD25 (1-164)- L20-hIL-2 (D20I) HC | EVQLVESGGGLVQPGRSLKLSCAVSGETESDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGRET ISRDNAKITLYLQMDSLRSEDATYYCARHGSGYFDYWGQGMVTVSSASTKGPSVFPPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSIIGTQTYICNVNHKPS NTKVDKKEVEPKSCDKTHTCPPCPAPELGGPSVFLFPPKPKDTLMI SRTPTEVTCVVVDVSHEDPEVKEN WYVDGVEVHNAKTKPREEQYNSYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPRE PQVYITLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDK SRWQQGNVSCSVMHEALHNNHYTQKLSLSLSPGKSGGGSELCDDDDPPEIPHATFKAMAYKEGTMLNCEC KRGFRRIKSGSLYMLCTGNSHSSWDNQCQCTSSATRNTTKQVTPQPEEQKERKTEMQSPMQPVDQAS LPGHCREPPPWENEATERIYHFVVGQMVYQCVQGYRALHRGPAESVCKMTHGKTRWTPQLICTSGGG GSGGGSGGGSGGGSAPTSSTTKTQLQLEHLLLDLQMLNGINNYKPNKLTTRMLTFKPYMPKKATEL KHLQCLEEELKPLEEVINLAQSKNPHLRPRDLISNINVI VLELKGSETTFMCEYADETATIVFELNRWI TFCQSIISTET |
| 589 | 1H3-hIgG1-L6- hCD25 (1-164)- L20-hIL-2 (D20S) HC | EVQLVESGGGLVQPGRSLKLSCAVSGFTFSDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGRET ISRDNAKITLYLQMDSLRSEDATYYCARHGSGYFDYWGQGMVTVSSASTKGPSVFPPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSIIGTQTYICNVNHKPS NTKVDKKEVEPKSCDKTHTCPPCPAPELGGPSVFLFPPKPKDTLMI SRTPTEVTCVVVDVSHEDPEVKEN WYVDGVEVHNAKTKPREEQYNSYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPRE PQVYITLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDK SRWQQGNVSCSVMHEALHNNHYTQKLSLSLSPGKSGGGSELCDDDDPPEIPHATFKAMAYKEGTMLNCEC KRGFRRIKSGSLYMLCTGNSHSSWDNQCQCTSSATRNTTKQVTPQPEEQKERKTEMQSPMQPVDQAS LPGHCREPPPWENEATERIYHFVVGQMVYQCVQGYRALHRGPAESVCKMTHGKTRWTPQLICTSGGG GSGGGSGGGSGGGSAPTSSTTKTQLQLEHLLLDLQMLNGINNYKPNKLTTRMLTFKPYMPKKATEL KHLQCLEEELKPLEEVINLAQSKNPHLRPRDLISNINVI VLELKGSETTFMCEYADETATIVFELNRWI TFCQSIISTLT |
| 590 | 1H3-hIgG1-L6- hCD25 (1-164)- L20-hIL-2 (D20H) HC | EVQLVESGGGLVQPGRSLKLSCAVSGFTESDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGRET ISRDNAKITLYLQMDSLRSEDATYYCARHGSGYFDYWGQGMVTVSSASTKGPSVFPPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSIIGTQTYICNVNHKPS NTKVDKKEVEPKSCDKTHTCPPCPAPELGGPSVFLFPPKPKDTLMI SRTPTEVTCVVVDVSHEDPEVKEN WYVDGVEVHNAKTKPREEQYNSYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPRE PQVYITPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDK SRWQQGNVSCSVMHEALHNNHYTQKLSLSLSPGKSGGGSELCDDDDPPEIPHATFKAMAYKEGTMLNCEC KRGFRRIKSGSLYMLCTGNSHSSWDNQCQCTSSATRNTTKQVTPQPEEQKERKTEMQSPMQPVDQAS LPGHCREPPPWENEATERIYHFVVGQMVYQCVQGYRALHRGPAESVCKMTHGKTRWTPQLICTSGGG GSGGGSGGGSGGGSAPTSSTTKTQLQLEHLLLDLQMLNGINNYKPNKLTTRMLTFKPYMPKKATEL KHLQCLEEELKPLEEVINLAQSKNPHLRPRDLISNINVI VLELKGSETTFMCEYADETATIVFELNRWI TFCQSIISTLT |
| 591 | 1H3-hIgG1-L6- hCD25 (1-164)- L20-hIL-2 (D20W) HC | EVQLVESGGGLVQPGRSILKLSCAVSGETESDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGRET ISRDNAKITLYLQMDSLRSEDATYYCARHGSGYFDYWGQGMVTVSSASTKGPSVFPPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSIIGTQTYICNVNHKPS NTKVDKKEVEPKSCDKTHTCPPCPAPELGGPSVFLFPPKPKDTLMI SRTPTEVTCVVVDVSHEDPEVKEN WYVDGVEVHNAKTKPREEQYNSYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPRE PQVYITLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDK SRWQQGNVSCSVMHEALHNNHYTQKLSLSLSPGKSGGGSELCDDDDPPEIPHATFKAMAYKEGTMLNCEC KRGFRRIKSGSLYMLCTGNSHSSWDNQCQCTSSATRNTTKQVTPQPEEQKERKTEMQSPMQPVDQAS LPGHCREPPPWENEATERIYHFVVGQMVYQCVQGYRALHRGPAESVCKMTHGKTRWTPQLICTSGGG GSGGGSGGGSGGGSAPTSSTTKTQLQLEHLLLDLQMLNGINNYKPNKLTTRMLTFKPYMPKKATEL KHLQCLEEELKPLEEVINLAQSKNPHLRPRDLISNINVI VLELKGSETTFMCEYADETATIVFELNRWI TFCQSIISTLT |

TABLE 29-continued

| Sequences | | |
|------------|--|---|
| SEQ ID NO: | Name | Sequence |
| 592 | 1H3-hIgG1-L6-hCD25 (1-164)-L20-hIL-2 (D20Y) HC | EVQLVESGGGLVQPGRSLKLSCAVSGFTFSDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGGRFT ISRDNAKITLYLQMDSLRSEDATATYYCARHGSGYFDYWGQGMVTVSSASTKGPSVFPPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPS NTKVDKKEVEPKSCDKTHTCPPCPAPELGGPSVFLFPPKPKDTLMI SRTP E V T C V V D V S H E D P E V K E N WYVDGVEVHNAKTKPREEQYNS TYRVVSVLTVLHQDWINGKEYKCKVSNKALPAPIEKTISKAKGQPRE PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSPFLYSKLTVDK SRWQQGNVPSCSVMHEALHNHYTQKSLSLSPGKSGGGGSELCDDDPPEIPHATFKAMAYKEGTMINCEC KRGFRRIKSGSLYMLCTGNS SHSSWDNQCQCTSSATRNTTKQVTPQPEEQKERKKTTEMQSPMPQVDQAS LPGHCREPPPWENEATERIYHFVVGQMVVYQCVQGYRALHRGPAESVCKMTHGKTRWTQPQLICTSGGG GSGGGGSGGGGSGGGSAPTSSTTKTQLQLEHLLLYLQMLNGINNYKNPKLTRMLTFKPYMPKKA TEL KHLQCLEEBELKPLEEVLNLAQSKNPHLRPRDLISNINVI VLELKGSETTFMCEYADETATIV EFLNRWI TFCQSIISTLT |
| 593 | 1H3-hIgG1-L6-hCD25 (1-164)-L20-hIL-2 (D20R) HC | EVQLVESGGGLVQPGRSLKLSCAVSGFTFSDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGGRFT ISRDNAKITLYLQMDSLRSEDATATYYCARHGSGYFDYWGQGMVTVSSASTKGPSVFPPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPS NTKVDKKEVEPKSCDKTHTCPPCPAPELGGPSVFLFPPKPKDTLMI SRTP E V T C V V D V S H E D P E V K E N WYVDGVEVHNAKTKPREEQYNS TYRVVSVLTVLHQDWINGKEYKCKVSNKALPAPIEKTISKAKGQPRE PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSPFLYSKLTVDK SRWQQGNVPSCSVMHEALHNHYTQKSLSLSPGKSGGGGSELCDDDPPEIPHATFKAMAYKEGTMINCEC KRGFRRIKSGSLYMLCTGNS SHSSWDNQCQCTSSATRNTTKQVTPQPEEQKERKKTTEMQSPMPQVDQAS LPGHCREPPPWENEATERIYHFVVGQMVVYQCVQGYRALHRGPAESVCKMTHGKTRWTQPQLICTSGGG GSGGGGSGGGGSGGGSAPTSSTTKTQLQLEHLLLYLQMLNGINNYKNPKLTRMLTFKPYMPKKA TEL KHLQCLEEBELKPLEEVLNLAQSKNPHLRPRDLISNINVI VLELKGSETTFMCEYADETATIV EFLNRWI TFCQSIISTLT |
| 594 | 1H3-hIgG1-L6-hCD25 (1-164)-L20-hIL-2 (D20F) HC | EVQLVESGGGLVQPGRSLKLSCAVSGFTFSDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGGRFT ISRDNAKITLYLQMDSLRSEDATATYYCARHGSGYFDYWGQGMVTVSSASTKGPSVFPPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPS NTKVDKKEVEPKSCDKTHTCPPCPAPELGGPSVFLFPPKPKDTLMI SRTP E V T C V V D V S H E D P E V K E N WYVDGVEVHNAKTKPREEQYNS TYRVVSVLTVLHQDWINGKEYKCKVSNKALPAPIEKTISKAKGQPRE PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSPFLYSKLTVDK SRWQQGNVPSCSVMHEALHNHYTQKSLSLSPGKSGGGGSELCDDDPPEIPHATFKAMAYKEGTMINCEC KRGFRRIKSGSLYMLCTGNS SHSSWDNQCQCTSSATRNTTKQVTPQPEEQKERKKTTEMQSPMPQVDQAS LPGHCREPPPWENEATERIYHFVVGQMVVYQCVQGYRALHRGPAESVCKMTHGKTRWTQPQLICTSGGG GSGGGGSGGGGSGGGSAPTSSTTKTQLQLEHLLLYLQMLNGINNYKNPKLTRMLTFKPYMPKKA TEL KHLQCLEEBELKPLEEVLNLAQSKNPHLRPRDLISNINVI VLELKGSETTFMCEYADETATIV EFLNRWI TFCQSIISTIT |
| 595 | 1H3-hIgG1-L6-hCD25 (1-164)-L20-hIL-2 (D84K) HC | EVQLVESGGGLVQPGRSLKLSCAVSGFTFSDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGGRFT ISRDNAKITLYLQMDSLRSEDATATYYCARHGSGYFDYWGQGMVTVSSASTKGPSVFPPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPS NTKVDKKEVEPKSCDKTHTCPPCPAPELGGPSVFLFPPKPKDTLMI SRTP E V T C V V D V S H E D P E V K E N WYVDGVEVHNAKTKPREEQYNS TYRVVSVLTVLHQDWINGKEYKCKVSNKALPAPIEKTISKAKGQPRE PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSPFLYSKLTVDK SRWQQGNVPSCSVMHEALHNHYTQKSLSLSPGKSGGGGSELCDDDPPEIPHATFKAMAYKEGTMINCEC KRGFRRIKSGSLYMLCTGNS SHSSWDNQCQCTSSATRNTTKQVTPQPEEQKERKKTTEMQSPMPQVDQAS LPGHCREPPPWENEATERIYHFVVGQMVVYQCVQGYRALHRGPAESVCKMTHGKTRWTQPQLICTSGGG GSGGGGSGGGGSGGGSAPTSSTTKTQLQLEHLLLYLQMLNGINNYKNPKLTRMLTFKPYMPKKA TEL KHLQCLEEBELKPLEEVLNLAQSKNPHLRPRDLISNINVI VLELKGSETTFMCEYADETATIV EFLNRWI TFCQSIISTLT |
| 596 | 1H3-hIgG1-L6-hCD25 (1-164)-L20-hIL-2 (S87A) HC | EVQLVESGGGLVQPGRSLKLSCAVSGFTESDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGRET ISRDNAKITLYLQMDSLRSEDATATYYCARHGSGYFDYWGQGMVTVSSASTKGPSVFPPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSSVTVPSSSI GTQTYICNVNHKPS NTKVDKKEVEPKSCDKTHTCPPCPAPELGGPSVFLFPPKPKDTLMI SRTP E V T C V V D V S H E D P E V K E N WYVDGVEVHNAKTKPREEQYNS TYRVVSVLTVLHQDWINGKEYKCKVSNKALPAPIEKTISKAKGQPRE PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSPFLYSKLTVDK SRWQQGNVPSCSVMHEALHNHYTQKSLSLSPGKSGGGGSELCDDDPPEIPHATFKAMAYKEGTMINCEC KRGFRRIKSGSLYMLCTGNS SHSSWDNQCQCTSSATRNTTKQVTPQPEEQKERKKTTEMQSPMPQVDQAS LPGHCREPPPWENEATERIYHFVVGQMVVYQCVQGYRALHRGPAESVCKMTHGKTRWTQPQLICTSGGG GSGGGGSGGGGSGGGSAPTSSTTKTQLQLEHLLLYLQMLNGINNYKNPKLTRMLTFKPYMPKKA TEL KHLQCLEEBELKPLEEVLNLAQSKNPHLRPRDLISNINVI VLELKGSETTFMCEYADETATIV EFLNRWI TFCQSIISTLT |
| 597 | 1H3-hIgG1-L6-hCD25 (1-164)-L20-hIL-2 (N88Y) HC | EVQLVESGGGLVQPGRSLKLSCAVSGETESDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGRET ISRDNAKITLYLQMDSLRSEDATATYYCARHGSGYEDYWGQGMVTVSSASTKGPSVFPPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSSVTVPSSSI GTQTYICNVNHKPS NTKVDKKEVEPKSCDKTHTCPPCPAPELGGPSVFLFPPKPKDTLMI SRTP E V T C V V D V S H E D P E V K E N WYVDGVEVHNAKTKPREEQYNS TYRVVSVLTVLHQDWINGKEYKCKVSNKALPAPIEKTISKAKGQPRE PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSPFLYSKLTVDK SRWQQGNVPSCSVMHEALHNHYTQKSLSLSPGKSGGGGSELCDDDPPEIPHATFKAMAYKEGTMINCEC KRGFRRIKSGSLYMLCTGNS SHSSWDNQCQCTSSATRNTTKQVTPQPEEQKERKKTTEMQSPMPQVDQAS LPGHCREPPPWENEATERIYHFVVGQMVVYQCVQGYRALHRGPAESVCKMTHGKTRWTQPQLICTSGGG |

TABLE 29-continued

| Sequences | | |
|------------|--|--|
| SEQ ID NO: | Name | Sequence |
| | | GGGGGGGGGGGGGGGAPTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKL TRMLTEKFYMPKKATEL KHLQCLEEBELKPLEEVINLAQSKNFHLRPRDLISYINVI VLELKGSETTEMCEYADETATIV EFLNRWI IFCQSIISTIT |
| 598 | 1H3-hIgG1-L6-hCD25 (1-164)-L20-hIL-2 (N88D) HC | EVQLVESGGGLVQPGRSLKLSCAVSGFTFSDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGGRFT ISRDNAKITLYLQMDSLRSEDATYYCARHGSGYFDYWGQGMVTVSSASTKGPSVFPPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYI CNVNHKPS NTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTP EVTCVVVDVSHEDPEVKEN WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPRE PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSPFLYSKLTVDK SRWQQGNVSCSVMHEALHNHYTQKSLSLSPGKSGGGGSELCDDDPPEIPHATFKAMAYKEGTMLNCEC KRGFRRIKSGSLYMLCTGNS SHSSWDNQCQCTSSATRNTTKQVTPQPEEQKERKKTTEMQSPMPVDQAS LPGHCREPPPWENEATERIYHFVVGQMVYQCVQGYRALHRGPAESVCKMTHGKTRWTQPQLICTSGGG GGGGGGGGGGGGGGGAPTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKL TRMLTFKFYMPKKATEL KHLQCLEEBELKPLEEVINLAQSKNFHLRPRDLISYINVI VLELKGSETTEMCEYADETATIV EFLNRWI TFCQSIISTIT |
| 599 | 1H3-hIgG1-L6-hCD25 (1-164)-L20-hIL-2 (N88R) HC | EVQLVESGGGLVQPGRSLKLSCAVSGFTFSDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGGRFT ISRDNAKITLYLQMDSLRSEDATYYCARHGSGYFDYWGQGMVTVSSASTKGPSVFPPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYI CNVNHKPS NTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTP EVTCVVVDVSHEDPEVKEN WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWINGKEYKCKVSNKALPAPI EKTISKAKGQPRE PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSPFLYSKLTVDK SRWQQGNVSCSVMHEALHNHYTQKSLSLSPGKSGGGGSELCDDDPPEIPHATFKAMAYKEGTMINCEC KRGFRRIKSGSLYMLCTGNS SHSSWDNQCQCTSSATRNTTKQVTPQPEEQKERKKTTEMQSPMPVDQAS LPGHCREPPPWENEATERIYHFVVGQMVYQCVQGYRALHRGPAESVCKMTHGKTRWTQPQLICTSGGG GGGGGGGGGGGGGGGAPTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKL TRMLTFKFYMPKKATEL KHLQCLEEBELKPLEEVINLAQSKNFHLRPRDLISYINVI VLELKGSETTEMCEYADETATIV EFLNRWI TFCQSIISTIT |
| 600 | 1H3-hIgG1-L6-hCD25 (1-164)-L20-hIL-2 (N88E) HC | EVQLVESGGGLVQPGRSLKLSCAVSGFTESDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGRET ISRDNAKITLYLQMDSLRSEDATYYCARHGSGYFDYWGQGMVTVSSASTKGPSVFPPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYI CNVNHKPS NTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTP EVTCVVVDVSHEDPEVKEN WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWINGKEYKCKVSNKALPAPI EKTISKAKGQPRE PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSPFLYSKI TVDK SRWQQGNVSCSVMHEALHNHYTQKSLSLSPGKSGGGGSELCDDDPPEIPHATFKAMAYKEGTMINCEC KRGFRRIKSGSLYMLCTGNS SHSSWDNQCQCTSSATRNTTKQVTPQPEEQKERKKTTEMQSPMPVDQAS IPGHCREPPPWENEATERIYHFVVGQMVYQCVQGYRALHRGPAESVCKMTHGKTRWTQPQLICTSGGG GGGGGGGGGGGGGGGAPTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKL TRMLTFKFYMPKKATEL KHLQCLEEBELKPLEEVINLAQSKNFHLRPRDLISEINVI VLELKGSETTEMCEYADETATIV EFLNRWI TFCQSIISTIT |
| 601 | 1H3-hIgG1-L6-hCD25 (1-164)-L20-hIL-2 (N88F) HC | EVQLVESGGGLVQPGRSLKLSCAVSGFTFSDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGRET ISRDNAKITLYLQMDSLRSEDATYYCARHGSGYFDYWGQGMVTVSSASTKGPSVFPPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYI CNVNHKPS NTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTP EVTCVVVDVSHEDPEVKEN WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI EKTISKAKGQPRE PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSPFLYSKLTVDK SRWQQGNVSCSVMHEALHNHYTQKSLSLSPGKSGGGGSELCDDDPPEIPHATFKAMAYKEGTMLNCEC KRGFRRIKSGSLYMLCTGNS SHSSWDNQCQCTSSATRNTTKQVTPQPEEQKERKKTTEMQSPMPVDQAS LPGHCREPPPWENEATERIYHFVVGQMVYQCVQGYRALHRGPAESVCKMTHGKTRWTQPQLICTSGGG GGGGGGGGGGGGGGGAPTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKL TRMLTFKFYMPKKATEL KHLQCLEEBELKPLEEVINLAQSKNFHLRPRDLISYINVI VLELKGSETTEMCEYADETATIV EFLNRWI TFCQSIISTIT |
| 602 | 1H3-hIgG1-L6-hCD25 (1-164)-L20-hIL-2 (N88I) HC | EVQLVESGGGLVQPGRSLKLSCAVSGFTFSDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGGRFT ISRDNAKITLYLQMDSLRSEDATYYCARHGSGYFDYWGQGMVTVSSASTKGPSVFPPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYI CNVNHKPS NTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTP EVTCVVVDVSHEDPEVKEN WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWINGKEYKCKVSNKALPAPI EKTISKAKGQPRE PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSPFLYSKLTVDK SRWQQGNVSCSVMHEALHNHYTQKSLSLSPGKSGGGGSELCDDDPPEIPHATFKAMAYKEGTMLNCEC KRGFRRIKSGSLYMLCTGNS SHSSWDNQCQCTSSATRNTTKQVTPQPEEQKERKKTTEMQSPMPVDQAS LPGHCREPPPWENEATERIYHFVVGQMVYQCVQGYRALHRGPAESVCKMTHGKTRWTQPQLICTSGGG GGGGGGGGGGGGGGGAPTSSSTKKTQLQLEHLLLDLQMLNGINNYKNPKL TRMLTFKFYMPKKATEL KHLQCLEEBELKPLEEVINLAQSKNFHLRPRDLISYINVI VLELKGSETTEMCEYADETATIV EFLNRWI TFCQSIISTIT |
| 603 | 1H3-hIgG1-L6-hCD25 (1-164)-L20-hIL-2 (I92A) HC | EVQLVESGGGLVQPGRSLKLSCAVSGFTFSDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGRET ISRDNAKITLYLQMDSLRSEDATYYCARHGSGYFDYWGQGMVTVSSASTKGPSVFPPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYI CNVNHKPS NTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMI SRTP EVTCVVVDVSHEDPEVKEN WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWINGKEYKCKVSNKALPAPI EKTISKAKGQPRE PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSPFLYSKLTVDK |

TABLE 29-continued

| Sequences | | |
|------------|--|--|
| SEQ ID NO: | Name | Sequence |
| | | SRWQQGNVFS CSCVMHEALHNHYTQKLSLSLSPGKSGGGGSELCDDDPPEIPHATFKAMAYKEGTMINCEC KRGERRIKSGSLYMLCTGNS SHSSWDNQCCQTS SATRNTTKQVTPQPEEQKERKTEMQSPMQPVDQAS LPGHCREPPPWENEATERIYHFVVGQMVY YQCVQGYRALHRGPAESVC KMTHTGKTRWTPQLICTSGGG GGGGGGGGGGSGGSAPTSSSTKKTQLQLEHLLIDLQMI LNGINNYKNPKLTRMLTFKPYMPKKATEL KHLQCLEEBELKPLEEVINLAQSKNFHLRPRDLISININVAIVLELKGSETTFMCEYADETATIVEFLNRWI TFCQSIISTIT |
| 604 | 1H3-hIgG1-L6-hCD25 (1-164)-L20-hIL-2 (E95A) HC | EVQLVESGGGLVQPGRS LKLSCAVSGFTFSDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGRFT ISRDNAKITLYLQMDSLRSEDATATYYCARHSGGYFDYWGQGMVTVSSASTKGPSVFPPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPS NTKVDKKEPKSCDKTHTCPCPAPEL LGGPSVFLFPPPKPDTLMI SRTP EVTCVVVDVSHEDPEVKEN WYVDGVEVHNAKTKPREEQYNS TYRVVSVLTVLHQDWINGKEYKCKVSNKALPAPIEKTISKAKGQPRE PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSPFLYSKLTVDK SRWQQGNVESCVMHEALHNHYTQKLSLSLSPGKSGGGGSELCDDDPPEIPHATFKAMAYKEGTMINCEC KRGERRIKSGSLYMLCTGNS SHSSWDNQCCQTS SATRNTTKQVTPQPEEQKERKTEMQSPMQPVDQAS LPGHCREPPPWENEATERIYHFVVGQMVY YQCVQGYRALHRGPAESVC KMTHTGKTRWTPQLICTSGGG GGGGGGGGGGSGGSAPTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTFKPYMPKKATEL KHLQCLEEBELKPLEEVINLAQSKNFHLRPRDLISININVAIVLALKGSETTFMCEYADETATIVEFLNRWI TFCQSIISTLT |
| 605 | 1H3-hIgG1-L6-hCD25 (1-164)-L20-hIL-2 (E95K) HC | EVQLVESGGGLVQPGRS LKLSCAVSGFTFSDYAMAVRQAPKKGLEWVATISYDGSRTYYRDSVKGRFT ISRDNAKITLYLQMDSLRSEDATATYYCARHSGGYFDYWGQGMVTVSSASTKGPSVFPPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPS NTKVDKKEPKSCDKTHTCPCPAPEL LGGPSVFLFPPPKPDTLMI SRTP EVTCVVVDVSHEDPEVKEN WYVDGVEVHNAKTKPREEQYNS TYRVVSVLTVLHQDWINGKEYKCKVSNKALPAPIEKTISKAKGQPRE PQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSPFLYSKLTVDK SRWQQGNVFS CSCVMHEALHNHYTQKLSLSLSPGKSGGGGSELCDDDPPEIPHATFKAMAYKEGTMINCEC KRGERRIKSGSLYMLCTGNS SHSSWDNQCCQTS SATRNTTKQVTPQPEEQKERKTEMQSPMQPVDQAS LPGHCREPPPWENEATERIYHFVVGQMVY YQCVQGYRALHRGPAESVC KMTHTGKTRWTPQLICTSGGG GGGGGGGGGGSGGSAPTSSSTKKTQLQLEHLLLDLQMI LNGINNYKNPKLTRMLTFKPYMPKKATEL KHLQCLEEBELKPLEEVINLAQSKNFHLRPRDLISININVAIVLKLKGSETTFMCEYADETATIVEFLNRWI TFCQSIISTLT |
| 606 | hIL-2 D20R/R38E | APTSSSTKKTQLQLEHLLRLQMI LNGINNYKNPKL EMLTFKPYMPKKATEL KHLQCLEEBELKPLEEV LNLAQSKNFHLRPRDLISININVAIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSIISTLT |
| 607 | hIL-2 D20N/R38E | APTSSSTKKTQLQLEHLLNLQMI LNGINNYKNPKL EMLTFKPYMPKKATEL KHLQCLEEBELKPLEEV LNLAQSKNFHLRPRDLISININVAIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSIISTLT |
| 608 | hIL-2 D20Q/R38E | APTSSSTKKTQLQLEHLLQLQMI LNGINNYKNPKL EMLTFKPYMPKKATEL KHLQCLEEBELKPLEEV LNLAQSKNFHLRPRDLISININVAIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSIISTLT |
| 609 | hIL-2 D20E/R38E | APTSSSTKKTQLQLEHLLLELQMI LNGINNYKNPKL EMLTFKPYMPKKATEL KHLQCLEEBELKPLEEV LNLAQSKNFHLRPRDLISININVAIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSIISTLT |
| 610 | hIL-2 D20G/R38E | APTSSSTKKTQLQLEHLLLGLQMI LNGINNYKNPKL EMLTFKPYMPKKATEL KHLQCLEEBELKPLEEV LNLAQSKNFHLRPRDLISININVAIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSIISTLT |
| 611 | hIL-2 D20I/R38E | APTSSSTKKTQLQLEHLLLIQMI LNGINNYKNPKL EMLTFKPYMPKKATEL KHLQCLEEBELKPLEEV LNLAQSKNFHLRPRDLISININVAIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSIISTLT |
| 612 | hIL-2 D20L/R38E | APTSSSTKKTQLQLEHLLLLQMI LNGINNYKNPKL EMLTFKPYMPKKATEL KHLQCLEEBELKPLEEV LNLAQSKNFHLRPRDLISININVAIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSIISTLT |
| 613 | hIL-2 D20K/R38E | APTSSSTKKTQLQLEHLLKLQMI LNGINNYKNPKL EMLTFKPYMPKKATEL KHLQCLEEBELKPLEEV LNLAQSKNFHLRPRDLISININVAIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSIISTLT |
| 614 | hIL-2 D20M/R38E | APTSSSTKKTQLQLEHLLMLQMI LNGINNYKNPKL EMLTFKPYMPKKATEL KHLQCLEEBELKPLEEV LNLAQSKNFHLRPRDLISININVAIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSIISTLT |
| 615 | hIL-2 D20F/R38E | APTSSSTKKTQLQLEHLLFLQMI LNGINNYKNPKL EMLTFKPYMPKKATEL KHLQCLEEBELKPLEEV LNLAQSKNFHLRPRDLISININVAIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSIISTLT |
| 616 | hIL-2 D20P/R38E | APTSSSTKKTQLQLEHLLPLQMI LNGINNYKNPKL EMLTFKPYMPKKATEL KHLQCLEEBELKPLEEV LNLAQSKNFHLRPRDLISININVAIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSIISTLT |
| 617 | hIL-2 D20T/R38E | APTSSSTKKTQLQLEHLLTLQMI LNGINNYKNPKL EMLTFKPYMPKKATEL KHLQCLEEBELKPLEEV LNLAQSKNFHLRPRDLISININVAIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSIISTLT |
| 618 | hIL-2 D20W/R38E | APTSSSTKKTQLQLEHLLWLQMI LNGINNYKNPKL EMLTFKPYMPKKATEL KHLQCLEEBELKPLEEV LNLAQSKNFHLRPRDLISININVAIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSIISTLT |
| 619 | hIL-2 D20Y/R38E | APTSSSTKKTQLQLEHLLYLQMI LNGINNYKNPKL EMLTFKPYMPKKATEL KHLQCLEEBELKPLEEV LNLAQSKNFHLRPRDLISININVAIVLELKGSETTFMCEYADETATIVEFLNRWITFCQSIISTLT |

TABLE 29-continued

| Sequences | | |
|------------|-------------------------|---|
| SEQ ID NO: | Name | Sequence |
| 620 | hIL-2 D20V/R38E | APTSSSTKKTQLQLEHLLLVLQMI L N G I N N Y K N P K L T E M L T P K F Y M P K K A T E L K H L Q C L E E E L K P L E E V L N L A Q S K N F H L R P R D L I S N I N V I V L E L K G S E T E M C E Y A D E T A T I V E F L N R W I T F C Q S I I S T L T |
| 621 | hIL-2 F42K/Y45R/V69R | APTSSSTKKTQLQLEHLLLDLQMI L N G I N N Y K N P K L T R M L T K K F R M P K K A T E L K H L Q C L E E E L K P L E E R L N L A Q S K N F H L R P R D L I S N I N V I V L E L K G S E T E M C E Y A D E T A T I V E F L N R W I T F C Q S I I S T L T |

EMBODIMENTS

The following list of embodiments is intended to complement, rather than displace or supersede, the previous descriptions.

Embodiment 1. A modified human interleukin-2 (hIL-2) protein, comprising a substitution at amino acid position 20 and a substitution at amino acid position 38 relative to the non-modified hIL-2 amino acid sequence of SEQ ID NO: 345, wherein the modified hIL-2 protein exhibits reduced potency on both a high affinity hIL-2 receptor and on an intermediate affinity hIL-2 receptor relative to a non-modified hIL-2.

Embodiment 2. The modified hIL-2 protein of embodiment 1, wherein the substitution at amino acid position 20 is selected from a D20A, D20S, D20Q, D20M, D20I, D20V, D20N, D20G, D20T, or D20E substitution.

Embodiment 3. The modified hIL-2 protein of embodiment 1 or 2, wherein the substitution at amino acid position 38 is selected from an R38E, R38N, R38G, R38H, R38I, R38L, R38M, R38F, R38P, R38S, R38T, R38W, R38Y, R38V, R38A, R38Q, R38D, and R38K substitution.

Embodiment 4. The modified hIL-2 protein of any one of the previous embodiments, further comprising a deletion or substitution at amino acid position 3 relative to the non-modified hIL-2 amino acid sequence of SEQ ID NO: 345.

Embodiment 5. The modified hIL-2 protein of embodiment 4, wherein the substitution at amino acid position 3 is T3A.

Embodiment 6. The modified hIL-2 protein of any one of the previous embodiments, further comprising a deletion or substitution at amino acid position 125 relative to the non-modified hIL-2 amino acid sequence of SEQ ID NO: 345.

Embodiment 7. The modified hIL-2 protein of embodiment 6, wherein the substitution at amino acid position 125 is C125A.

Embodiment 8. The modified hIL-2 protein of any one of the previous embodiments, wherein the modified hIL-2 protein exhibits about a 1,000-fold reduction in potency on the high affinity IL-2 receptor (hIL-2R $\alpha\beta\gamma$).

Embodiment 9. The modified hIL-2 protein of any one of the previous embodiments, wherein the modified hIL-2 protein exhibits about a 10,000-fold reduction in potency on the intermediate affinity IL-2 receptor (hIL-2R $\beta\gamma$).

Embodiment 10. The modified hIL-2 protein of any one of embodiments 1 to 9, wherein the modified hIL-2 protein is fused to an anti-PD-1 antibody or an antigen-binding fragment thereof.

Embodiment 11. The modified hIL-2 protein of embodiment 10, wherein the modified hIL-2 protein is fused to the antibody or an antigen-binding fragment thereof at the N-terminus of an antibody light chain, the C-terminus of an antibody light chain, the N-terminus of an antibody heavy

chain, the C-terminus of an antibody heavy chain, the N-terminus of the antigen-binding fragment, or the C-terminus of the antigen-binding fragment.

Embodiment 12. The modified hIL-2 protein of embodiment 10 or 11, wherein the modified hIL-2 protein is directly fused by a peptide bond to the antibody or an antigen-binding fragment thereof.

Embodiment 13. The modified hIL-2 protein of embodiment 12, wherein the modified hIL-2 is directly fused by a peptide bond to the C-terminal amino acid residue of the antibody heavy chain.

Embodiment 14. The modified hIL-2 protein of embodiment 10 or 11, wherein the modified hIL-2 protein is fused to the antibody or an antigen-binding fragment thereof through a linker.

Embodiment 15. A modified human interleukin-2 (hIL-2) protein, comprising a D20A, D20S, D20Q, D20M, D20I, D20V, D20N, D20G, D20T, or D20E substitution at amino acid position 20 and a R38E substitution at amino acid position 38 relative to the non-modified hIL-2 amino acid sequence of SEQ ID NO: 345.

Embodiment 16. The modified hIL-2 protein of embodiment 15, comprising the amino acid sequence of any one of SEQ ID NOs: 307, 607-611, 614, 617, or 620.

Embodiment 17. The modified hIL-2 protein of embodiment 15 or 16, comprising a D20A substitution and a R38E substitution.

Embodiment 18. The modified hIL-2 protein of embodiment 17, comprising the amino acid sequence of SEQ ID NO: 149.

Embodiment 19. The modified hIL-2 protein of any one of embodiments 15-18, further comprising a deletion or substitution at amino acid position 3 relative to the non-modified hIL-2 amino acid sequence of SEQ ID NO: 345.

Embodiment 20. The modified hIL-2 protein of embodiment 19, wherein the substitution at amino acid position 3 is T3A.

Embodiment 21. The modified hIL-2 protein of embodiment 20, comprising the amino acid sequence of SEQ ID NO: 216.

Embodiment 22. The modified hIL-2 protein of embodiment 19, comprising the amino acid sequence of SEQ ID NO: 218.

Embodiment 23. The modified hIL-2 protein of any one of embodiments 15-22, further comprising a deletion or substitution at amino acid position 125 relative to the non-modified hIL-2 amino acid sequence of SEQ ID NO: 345.

Embodiment 24. The modified hIL-2 protein of embodiment 23, wherein the substitution at amino acid position 125 is C125A.

Embodiment 25. The modified hIL-2 protein of embodiment 24, comprising the amino acid sequence of SEQ ID NO: 215, 217, or 219.

Embodiment 26. The modified hIL-2 protein of embodiment 25, comprising the amino acid sequence of SEQ ID NO: 217.

Embodiment 27. The modified hIL-2 protein of any one of embodiments 15 to 26, wherein the modified hIL-2 protein is fused to an anti-PD-1 antibody or an antigen-binding fragment thereof.

Embodiment 28. The modified hIL-2 protein of embodiment 27, wherein the modified hIL-2 protein is fused to the antibody or an antigen-binding fragment thereof at the N-terminus of an antibody light chain, the C-terminus of an antibody light chain, the N-terminus of an antibody heavy chain, the C-terminus of an antibody heavy chain, the N-terminus of the antigen-binding fragment, or the C-terminus of the antigen-binding fragment.

Embodiment 29. The modified hIL-2 protein of embodiment 27 or 28, wherein the modified hIL-2 protein is directly fused by a peptide bond to the antibody or an antigen-binding fragment thereof.

Embodiment 30. The modified hIL-2 protein of embodiment 29, wherein the modified hIL-2 is directly fused by a peptide bond to the C-terminal amino acid residue of the antibody heavy chain.

Embodiment 31. The modified hIL-2 protein of embodiment 27 or 28, wherein the modified hIL-2 protein is fused to the antibody or an antigen-binding fragment thereof through a linker.

Embodiment 32. A human antibody molecule, or antigen-binding fragment thereof, that immunospecifically binds to human programmed cell death protein-1 (hPD-1), wherein the human antibody molecule or antigen-binding fragment thereof comprises:

- a) a heavy chain complementarity determining region 1 (CDR1) comprising the amino acid sequence of SEQ ID NO: 418, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 419, a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 420, a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 421, a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 422, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 423;
- b) a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 386, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 387, a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 388, a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 389, a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 390, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 391;
- c) a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 396, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 397, a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 398, a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 399, a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 400, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 401; or
- d) a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 406, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 407, a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 408, a light chain CDR1

comprising the amino acid sequence of SEQ ID NO: 409, a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 410, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 411.

Embodiment 33. The human antibody molecule, or antigen-binding fragment thereof, of embodiment 32, comprising:

- a) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 416 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 417;
- b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 384 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 385;
- c) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 394 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 395; or
- d) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 404 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 405.

Embodiment 34. The human antibody molecule, or antigen-binding fragment thereof, of embodiment 32 or 33, comprising a human IgG1 heavy chain constant region.

Embodiment 35. The human antibody molecule, or antigen-binding fragment thereof, of embodiment 34, comprising an L235A substitution and a G237A substitution, according to EU numbering.

Embodiment 36. The human antibody molecule, or antigen-binding fragment thereof, of any one of embodiments 32-35, comprising:

- a) a heavy chain comprising the amino acid sequence of SEQ ID NO: 414 and a light chain comprising the amino acid sequence of SEQ ID NO: 415;
- b) a heavy chain comprising the amino acid sequence of SEQ ID NO: 424 and a light chain comprising the amino acid sequence of SEQ ID NO: 425;
- c) a heavy chain comprising the amino acid sequence of SEQ ID NO: 426 and a light chain comprising the amino acid sequence of SEQ ID NO: 427; or
- d) a heavy chain comprising the amino acid sequence of SEQ ID NO: 428 and a light chain comprising the amino acid sequence of SEQ ID NO: 429.

Embodiment 37. The human antibody molecule, or antigen-binding fragment thereof, of embodiment 36, comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 414 and a light chain comprising the amino acid sequence of SEQ ID NO: 415.

Embodiment 38. The human antibody molecule, or antigen-binding fragment thereof, of any one of embodiments 32-37, fused to a modified human interleukin-2 (hIL-2) protein comprising a substitution at amino acid position 20 and a substitution at amino acid position 38 relative to the non-modified hIL-2 amino acid sequence of SEQ ID NO: 345.

Embodiment 39. The human antibody molecule, or antigen-binding fragment thereof, of embodiment 38, wherein the modified hIL-2 protein comprises the amino acid sequence of any one of SEQ ID NOs: 134-150, 307, 344, 607-611, 614, 617, or 620.

Embodiment 40. The human antibody molecule, or antigen-binding fragment thereof, of embodiment 39, wherein the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 149.

Embodiment 41. The human antibody molecule, or antigen-binding fragment thereof, of any one of embodiments 38-40, wherein the modified hIL-2 protein further comprises a deletion or substitution at amino acid position 3 relative to the non-modified hIL-2 amino acid sequence of SEQ ID NO: 345.

Embodiment 42. The human antibody molecule, or antigen-binding fragment thereof, of embodiment 41, wherein the substitution at amino acid position 3 is T3A.

Embodiment 43. The human antibody molecule, or antigen-binding fragment thereof, of embodiment 42, wherein the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 216.

Embodiment 44. The human antibody molecule, or antigen-binding fragment thereof, of embodiment 41, wherein the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 218.

Embodiment 45. The human antibody molecule, or antigen-binding fragment thereof, of any one of embodiments 38-44, wherein the modified hIL-2 protein further comprises a deletion or substitution at amino acid position 125 relative to the non-modified hIL-2 amino acid sequence of SEQ ID NO: 345.

Embodiment 46. The human antibody molecule, or antigen-binding fragment thereof, of embodiment 45, wherein the substitution at amino acid position 125 is C125A.

Embodiment 47. The human antibody molecule, or antigen-binding fragment thereof, of embodiment 46, wherein the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 215, 217, or 219.

Embodiment 48. The human antibody molecule, or antigen-binding fragment thereof, of embodiment 47, wherein the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 217.

Embodiment 49. The human antibody molecule, or antigen-binding fragment thereof, of any one of embodiments 38-48, wherein the modified hIL-2 protein is fused to the antibody or antigen-binding fragment thereof at the N-terminus of an antibody light chain, the C-terminus of an antibody light chain, the N-terminus of an antibody heavy chain, the C-terminus of an antibody heavy chain, the N-terminus of the antigen-binding fragment, or the C-terminus of the antigen-binding fragment.

Embodiment 50. The human antibody molecule, or antigen-binding fragment thereof, of any one of embodiments 38-49, wherein the modified hIL-2 protein is directly fused by a peptide bond to the antibody or antigen-binding fragment thereof.

Embodiment 51. The human antibody molecule, or antigen-binding fragment thereof, of embodiment 50, wherein the modified hIL-2 protein is directly fused by a peptide bond to the C-terminal amino acid residue of the antibody heavy chain.

Embodiment 52. The human antibody molecule, or antigen-binding fragment thereof, of any one of embodiments 38-49, wherein the modified hIL-2 protein is fused to the antibody or antigen-binding fragment through a linker.

Embodiment 53. An immunoconjugate comprising:

- (a) a modified human interleukin-2 (hIL-2) protein comprising a substitution at amino acid position 20 and a substitution at amino acid position 38 relative to the non-modified hIL-2 amino acid sequence of SEQ ID NO: 345; and
- (b) a human antibody molecule, or antigen-binding fragment thereof, that immunospecifically binds to human

programmed cell death protein-1 (hPD-1), wherein the human antibody molecule or antigen-binding fragment thereof comprises:

- (i) a heavy chain complementarity determining region 1 (CDR1) comprising the amino acid sequence of SEQ ID NO: 418, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 419, a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 420, a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 421, a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 422, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 423;
- (ii) a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 386, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 387, a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 388, a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 389, a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 390, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 391;
- (iii) a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 396, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 397, a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 398, a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 399, a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 400, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 401; or
- (iv) a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 406, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 407, a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 408, a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 409, a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 410, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 411.

Embodiment 54. The immunoconjugate of embodiment 53, wherein the substitution at amino acid position 20 of the modified hIL-2 protein is selected from a D20A, D20S, D20Q, D20M, D20I, D20V, D20N, D20G, D20T, or D20E substitution.

Embodiment 55. The immunoconjugate of embodiment 53 or 54, wherein the substitution at amino acid position 38 of the modified hIL-2 protein is selected from an R38E, R38N, R38G, R38H, R38I, R38L, R38M, R38F, R38P, R38S, R38T, R38W, R38Y, R38V, R38A, R38Q, R38D, and R38K substitution.

Embodiment 56. The immunoconjugate of any one of embodiments 53-55, wherein the substitution at amino acid position 20 of the modified hIL-2 protein is selected from a D20A, D20S, D20Q, D20M, D20I, D20V, D20N, D20G, D20T, or D20E substitution and the amino acid substitution at amino acid position 38 of the modified hIL-2 protein is R38E.

Embodiment 57. The immunoconjugate of any one of embodiments 53-56, wherein the modified hIL-2 protein comprises the amino acid sequence of any one of SEQ ID NOs: 134-150, 307, 344, 607-611, 614, 617, or 620.

Embodiment 58. The immunoconjugate of any one of embodiments 53-56, wherein the modified hIL-2 protein comprises a D20A and a R38E substitution.

Embodiment 59. The immunoconjugate of embodiment 58, wherein the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 149.

Embodiment 60. The immunoconjugate of any one of embodiments 53-57, comprising the amino acid sequence of any one of SEQ ID NOs: 608, 614, 611, 620, 607, 610, 617, 609, or 307.

Embodiment 61. The immunoconjugate of any one of embodiments 53-60, wherein the modified hIL-2 protein further comprises a deletion or substitution at amino acid position 3 relative to the non-modified hIL-2 amino acid sequence of SEQ ID NO: 345.

Embodiment 62. The immunoconjugate of embodiment 61, wherein the substitution at amino acid position 3 of the modified hIL-2 protein is T3A.

Embodiment 63. The immunoconjugate of embodiment 62, wherein the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 216.

Embodiment 64. The immunoconjugate of embodiment 61, wherein the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 218.

Embodiment 65. The immunoconjugate of any one of embodiments 53-64, wherein the modified hIL-2 protein further comprises a deletion or substitution at amino acid position 125 relative to the non-modified hIL-2 amino acid sequence of SEQ ID NO: 345.

Embodiment 66. The immunoconjugate of embodiment 65, wherein the substitution at amino acid position 125 is C125A.

Embodiment 67. The immunoconjugate of embodiment 66, wherein the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 215, 217, or 219.

Embodiment 68. The immunoconjugate of embodiment 67, wherein the modified hIL-2 protein comprises the amino acid sequence of SEQ ID NO: 217.

Embodiment 69. The immunoconjugate of any one of embodiments 53-68, wherein the modified hIL-2 protein is fused to the antibody or antigen-binding fragment thereof at the N-terminus of an antibody light chain, the C-terminus of an antibody light chain, the N-terminus of an antibody heavy chain, the C-terminus of an antibody heavy chain, the N-terminus of the antigen-binding fragment, or the C-terminus of the antigen-binding fragment.

Embodiment 70. The immunoconjugate of any one of embodiments 53-69, wherein the modified hIL-2 protein is directly fused by a peptide bond to the antibody or antigen-binding fragment thereof.

Embodiment 71. The immunoconjugate of embodiment 70, wherein modified hIL-2 protein is directly fused by a peptide bond to the C-terminal amino acid residue of the antibody heavy chain.

Embodiment 72. The immunoconjugate of any one of embodiments 53-69, wherein the modified hIL-2 protein is fused to the antibody or antigen-binding fragment thereof through a linker.

Embodiment 73. The immunoconjugate of any one of embodiments 53-72, wherein the human antibody molecule, or antigen-binding fragment thereof, comprises:

- a) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 416 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 417;

- b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 384 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 385;

- c) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 394 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 395; or

- d) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 404 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 405.

Embodiment 74. The immunoconjugate of any one of embodiments 53-73, wherein the human antibody molecule, or antigen-binding fragment thereof, comprises an IgG1 heavy chain constant region.

Embodiment 75. The immunoconjugate of embodiment 74, wherein the human antibody molecule, or antigen-binding fragment thereof, comprises an L235A substitution and a G237A substitution, according to EU numbering.

Embodiment 76. The immunoconjugate of any one of embodiments 53-75, wherein the human antibody molecule, or antigen-binding fragment thereof, comprises:

- a) a heavy chain comprising the amino acid sequence of SEQ ID NO: 414 and a light chain comprising the amino acid sequence of SEQ ID NO: 415;

- b) a heavy chain comprising the amino acid sequence of SEQ ID NO: 424 and a light chain comprising the amino acid sequence of SEQ ID NO: 425;

- c) a heavy chain comprising the amino acid sequence of SEQ ID NO: 426 and a light chain comprising the amino acid sequence of SEQ ID NO: 427; or

- d) a heavy chain comprising the amino acid sequence of SEQ ID NO: 428 and a light chain comprising the amino acid sequence of SEQ ID NO: 429.

Embodiment 77. The immunoconjugate of embodiment 76, wherein the human antibody molecule, or antigen-binding fragment thereof, comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 414 and a light chain comprising the amino acid sequence of SEQ ID NO: 415.

Embodiment 78. The immunoconjugate of any one of embodiments 53-77, comprising a light chain comprising the amino acid sequence of SEQ ID NO: 415; and a heavy chain-modified hIL-2 protein fusion comprising the amino acid sequence of SEQ ID NO: 532.

Embodiment 79. A pharmaceutical composition comprising the modified hIL-2 protein of any one of embodiments 1-31, the human antibody molecule, or antigen-binding fragment thereof, of any one of embodiments 32-52, or the immunoconjugate of any one of embodiments 53-78.

Embodiment 80. A polynucleotide, comprising a nucleic acid sequence encoding the modified hIL-2 protein of any one of embodiments 1-31, the human antibody molecule, or antigen-binding fragment thereof, of any one of embodiments 32-52, or the immunoconjugate of any one of embodiments 53-78.

Embodiment 81. A vector comprising a polynucleotide comprising a nucleic acid sequence that encodes the modified hIL-2 protein of any one of embodiments 1-31, the human antibody molecule, or antigen-binding fragment thereof, of any one of embodiments 32-52, or the immunoconjugate of any one of embodiments 53-78.

Embodiment 82. A transformed cell comprising the vector of embodiment 81.

Embodiment 83. A method of treating a disease or disorder in a subject, the method comprising administering a

therapeutically effective amount of the modified hIL-2 protein of any one of embodiments 10-14 and 27-31, the immunoconjugate of any one of embodiments 53-78, or the pharmaceutical composition of embodiment 79 to the subject to thereby treat the disease or disorder.

Embodiment 84. The method of embodiment 83, wherein the disease or disorder is cancer.

Embodiment 85. The method of embodiment 84, wherein the cancer is melanoma.

Embodiment 86. The method of embodiment 84, wherein the cancer is non-small cell lung carcinoma.

Embodiment 87. Use of the modified hIL-2 protein of any one of embodiments 10-14 and 27-31, the immunoconjugate of any one of embodiments 53-78, or the pharmaceutical composition of embodiment 79 in the preparation of a medicament for the treatment of a disease or disorder.

Embodiment 88. The use of embodiment 87, wherein the disease or disorder is cancer.

Embodiment 89. The use of embodiment 88, wherein the cancer is melanoma.

5 Embodiment 90. The use of embodiment 88, wherein the cancer is non-small cell lung carcinoma.

Embodiment 91. Use of the modified hIL-2 protein of any one of embodiments 10-14 and 27-31, the immunoconjugate of any one of embodiments 53-78, or the pharmaceutical composition of embodiment 79 for the treatment of a disease or disorder.

Embodiment 92. The use of embodiment 91, wherein the disease or disorder is cancer.

10 Embodiment 93. The use of embodiment 92, wherein the cancer is melanoma.

15 Embodiment 94. The use of embodiment 92, wherein the cancer is non-small cell lung carcinoma.

SEQUENCE LISTING

Sequence total quantity: 621

SEQ ID NO: 1 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 1
 APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TKKFYMPKKA TELKHLQCLE 60
 EELKPLEEVL NLAQSKNFHL RPRDLISIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 2 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 2
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 EELKPLEEAL NLAQSKNFHL RPRDLISIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 3 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 3
 APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
 EELKPLEEEL NLAQSKNFHL RPRDLISIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 4 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 4
 APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
 EELKPLEEFL NLAQSKNFHL RPRDLISIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 5 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 5
 APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
 EELKPLEEGL NLAQSKNFHL RPRDLISIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 6 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

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SEQUENCE: 6
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEHL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 7 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 7
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEHL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 8 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 8
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEKL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 9 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 9
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEELL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 10 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 10
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEML NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 11 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 11
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEQL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 12 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 12
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEESL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 13 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 13
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEETL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 14 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein

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                organism = Synthetic construct
SEQUENCE: 14
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 15      moltype = AA length = 133
FEATURE           Location/Qualifiers
source            1..133
                  mol_type = protein
                  organism = Synthetic construct

SEQUENCE: 15
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 16      moltype = AA length = 133
FEATURE           Location/Qualifiers
source            1..133
                  mol_type = protein
                  organism = Synthetic construct

SEQUENCE: 16
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 17      moltype = AA length = 133
FEATURE           Location/Qualifiers
source            1..133
                  mol_type = protein
                  organism = Synthetic construct

SEQUENCE: 17
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKKRMPPKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 18      moltype = AA length = 133
FEATURE           Location/Qualifiers
source            1..133
                  mol_type = protein
                  organism = Synthetic construct

SEQUENCE: 18
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TTKFYMPKKA TELKHLQCLE 60
EELKPLEERL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 19      moltype = AA length = 133
FEATURE           Location/Qualifiers
source            1..133
                  mol_type = protein
                  organism = Synthetic construct

SEQUENCE: 19
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFRMPKKA TELKHLQCLE 60
EELKPLEERL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 20      moltype = AA length = 133
FEATURE           Location/Qualifiers
source            1..133
                  mol_type = protein
                  organism = Synthetic construct

SEQUENCE: 20
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TTKKRMPPKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 21      moltype = AA length = 133
FEATURE           Location/Qualifiers
source            1..133
                  mol_type = protein
                  organism = Synthetic construct

SEQUENCE: 21
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTAML TTKFRMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 22      moltype = AA length = 133
FEATURE           Location/Qualifiers
source            1..133

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mol_type = protein
organism = Synthetic construct

SEQUENCE: 22
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TKKFRMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 23      moltype = AA length = 133
FEATURE           Location/Qualifiers
source            1..133
                  mol_type = protein
                  organism = Synthetic construct

SEQUENCE: 23
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TKEFRMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 24      moltype = AA length = 133
FEATURE           Location/Qualifiers
source            1..133
                  mol_type = protein
                  organism = Synthetic construct

SEQUENCE: 24
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TKTFRMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 25      moltype = AA length = 133
FEATURE           Location/Qualifiers
source            1..133
                  mol_type = protein
                  organism = Synthetic construct

SEQUENCE: 25
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TKKFRMPKKA TELKHLQCLE 60
EALKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 26      moltype = AA length = 133
FEATURE           Location/Qualifiers
source            1..133
                  mol_type = protein
                  organism = Synthetic construct

SEQUENCE: 26
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TKKFRMPKKA TELKHLQCLE 60
EELKRLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 27      moltype = AA length = 133
FEATURE           Location/Qualifiers
source            1..133
                  mol_type = protein
                  organism = Synthetic construct

SEQUENCE: 27
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TKKFRMPKKA TELKHLQCLE 60
EELKSLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 28      moltype = AA length = 133
FEATURE           Location/Qualifiers
source            1..133
                  mol_type = protein
                  organism = Synthetic construct

SEQUENCE: 28
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TKKFRMPKKA TELKHLQCLE 60
EELKPLEEAL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 29      moltype = AA length = 133
FEATURE           Location/Qualifiers
source            1..133
                  mol_type = protein
                  organism = Synthetic construct

SEQUENCE: 29
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TKKFRMPKKA TELKHLQCLE 60
EELKPLEEDL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 30      moltype = AA length = 133
FEATURE           Location/Qualifiers

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source                1..133
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 30
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TKKFRMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT                                           133

SEQ ID NO: 31         moltype = AA length = 133
FEATURE              Location/Qualifiers
source               1..133
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 31
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT                                           133

SEQ ID NO: 32         moltype = AA length = 133
FEATURE              Location/Qualifiers
source               1..133
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 32
APTSSSTKKT QLQLEHLLLN LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT                                           133

SEQ ID NO: 33         moltype = AA length = 133
FEATURE              Location/Qualifiers
source               1..133
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 33
APTSSSTKKT QLQLEHLLLK LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT                                           133

SEQ ID NO: 34         moltype = AA length = 133
FEATURE              Location/Qualifiers
source               1..133
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 34
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISAIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT                                           133

SEQ ID NO: 35         moltype = AA length = 133
FEATURE              Location/Qualifiers
source               1..133
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 35
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISGIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT                                           133

SEQ ID NO: 36         moltype = AA length = 133
FEATURE              Location/Qualifiers
source               1..133
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 36
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISHIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT                                           133

SEQ ID NO: 37         moltype = AA length = 133
FEATURE              Location/Qualifiers
source               1..133
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 37
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISKIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT                                           133

SEQ ID NO: 38         moltype = AA length = 133

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FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 38
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRALISIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 39 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 39
APTSSSTKKT QLQLAHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 40 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 40
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISIN VIVLALKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 41 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 41
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISAIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 42 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 42
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLIANIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 43 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 43
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRALISAIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 44 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 44
APTSSSTKKT QLQLAHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISAIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 45 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 45
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLIAAIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

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SEQ ID NO: 54 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 54
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFAFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 55 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 55
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFEFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 56 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 56
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFQFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 57 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 57
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFAMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 58 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 58
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFKMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 59 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 59
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFSMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 60 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 60
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFRMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 61 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 61
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
AELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120

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WITFCQSIIS TLT 133

SEQ ID NO: 62 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 62
 APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
 RELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 63 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 63
 APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
 KELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 64 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 64
 APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
 EALKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 65 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 65
 APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
 ERLKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 66 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 66
 APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
 EKLKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 67 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 67
 APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
 BYLKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 68 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 68
 APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
 BELKPLEYVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 69 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 69
 APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60

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EELKPLEAVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 70 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 70
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEKVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 71 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 71
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEKVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 72 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 72
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLELVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 73 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 73
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NYAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 74 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 74
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NRAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 75 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 75
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NDAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 76 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 76
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NDAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 77 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 77

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APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NHAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

```

```

SEQ ID NO: 78      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct

```

```

SEQUENCE: 78
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NHAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

```

```

SEQ ID NO: 79      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct

```

```

SEQUENCE: 79
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTDML TFKFYMPKKA TELKHLQCLE 60
RELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

```

```

SEQ ID NO: 80      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct

```

```

SEQUENCE: 80
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTDML TFEFYMPKKA TELKHLQCLE 60
RELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

```

```

SEQ ID NO: 81      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct

```

```

SEQUENCE: 81
APASSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TAKFAMPKKA TELKHLQCLE 60
EELKPLEEVL NGAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFAQSIIS TLT 133

```

```

SEQ ID NO: 82      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct

```

```

SEQUENCE: 82
APTSSSTKKT QLQLAHLLED LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

```

```

SEQ ID NO: 83      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct

```

```

SEQUENCE: 83
APTSSSTKKT QLQLRHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

```

```

SEQ ID NO: 84      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct

```

```

SEQUENCE: 84
APTSSSTKKT QLQLKHLLED LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

```

```

SEQ ID NO: 85      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct

```

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SEQUENCE: 85
APTSSSTKKT QLQLEALLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 86 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 86
APTSSSTKKT QLQLEALLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 87 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 87
APTSSSTKKT QLQLEALLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 88 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 88
APTSSSTKKT QLQLEHLLAD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 89 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 89
APTSSSTKKT QLQLEHLLLI LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 90 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 90
APTSSSTKKT QLQLEHLLLS LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 91 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 91
APTSSSTKKT QLQLEHLLH LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 92 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 92
APTSSSTKKT QLQLEHLLLT LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 93 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein

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                                organism = Synthetic construct
SEQUENCE: 93
APTSSSTKKT QLQLEHLLW LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 94      moltype = AA length = 133
FEATURE          Location/Qualifiers
source          1..133
                mol_type = protein
                organism = Synthetic construct

SEQUENCE: 94
APTSSSTKKT QLQLEHLLY LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 95      moltype = AA length = 133
FEATURE          Location/Qualifiers
source          1..133
                mol_type = protein
                organism = Synthetic construct

SEQUENCE: 95
APTSSSTKKT QLQLEHLLR LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 96      moltype = AA length = 133
FEATURE          Location/Qualifiers
source          1..133
                mol_type = protein
                organism = Synthetic construct

SEQUENCE: 96
APTSSSTKKT QLQLEHLLF LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 97      moltype = AA length = 133
FEATURE          Location/Qualifiers
source          1..133
                mol_type = protein
                organism = Synthetic construct

SEQUENCE: 97
APTSSSTKKT QLQLEHLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL APRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 98      moltype = AA length = 133
FEATURE          Location/Qualifiers
source          1..133
                mol_type = protein
                organism = Synthetic construct

SEQUENCE: 98
APTSSSTKKT QLQLEHLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRALISNIN VIVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 99      moltype = AA length = 133
FEATURE          Location/Qualifiers
source          1..133
                mol_type = protein
                organism = Synthetic construct

SEQUENCE: 99
APTSSSTKKT QLQLEHLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRRLISNIN VIVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 100     moltype = AA length = 133
FEATURE          Location/Qualifiers
source          1..133
                mol_type = protein
                organism = Synthetic construct

SEQUENCE: 100
APTSSSTKKT QLQLEHLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRKLISNIN VIVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 101     moltype = AA length = 133
FEATURE          Location/Qualifiers
source          1..133

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mol_type = protein
organism = Synthetic construct

SEQUENCE: 101
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLIANIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 102      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct

SEQUENCE: 102
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISYIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 103      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct

SEQUENCE: 103
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISDIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 104      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct

SEQUENCE: 104
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISRIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 105      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct

SEQUENCE: 105
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISEIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 106      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct

SEQUENCE: 106
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISFIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 107      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct

SEQUENCE: 107
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISIIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 108      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct

SEQUENCE: 108
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VAVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 109      moltype = AA length = 133
FEATURE           Location/Qualifiers

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source                1..133
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 109
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT                                             133

SEQ ID NO: 110        moltype = AA length = 133
FEATURE              Location/Qualifiers
source               1..133
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 110
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VSVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT                                             133

SEQ ID NO: 111        moltype = AA length = 133
FEATURE              Location/Qualifiers
source               1..133
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 111
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VFVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT                                             133

SEQ ID NO: 112        moltype = AA length = 133
FEATURE              Location/Qualifiers
source               1..133
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 112
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VRVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT                                             133

SEQ ID NO: 113        moltype = AA length = 133
FEATURE              Location/Qualifiers
source               1..133
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 113
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT                                             133

SEQ ID NO: 114        moltype = AA length = 133
FEATURE              Location/Qualifiers
source               1..133
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 114
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VEVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT                                             133

SEQ ID NO: 115        moltype = AA length = 133
FEATURE              Location/Qualifiers
source               1..133
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 115
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLALKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT                                             133

SEQ ID NO: 116        moltype = AA length = 133
FEATURE              Location/Qualifiers
source               1..133
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 116
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLRLKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT                                             133

SEQ ID NO: 117        moltype = AA length = 133

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FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 117
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLKLKGE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 118 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 118
APTSSSTKKT QLQLEHLLLY LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 119 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 119
APTSSSTKKT QLQLEALLLY LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 120 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 120
APTSSSTKKT QLQLEYLLLY LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 121 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 121
APTSSSTKKT QLQLEHLLLY LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VAVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 122 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 122
APTSSSTKKT QLQLEHLLLY LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VSVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 123 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 123
APTSSSTKKT QLQLEHLLLY LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VRVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 124 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 124
APTSSSTKKT QLQLEHLLLY LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLRKLGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

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SEQ ID NO: 133 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 133
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFKMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 134 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 134
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTNML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 135 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 135
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTGML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 136 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 136
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTHML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 137 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 137
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTIML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 138 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 138
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTLML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 139 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 139
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTMML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 140 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 140
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTFML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120

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WITFCQSIIS TLT 133

SEQ ID NO: 141 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 141
 APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTPLM TFKFYMPKKA TELKHLQCLE 60
 EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 142 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 142
 APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTSML TFKFYMPKKA TELKHLQCLE 60
 EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 143 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 143
 APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTTML TFKFYMPKKA TELKHLQCLE 60
 EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 144 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 144
 APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTWML TFKFYMPKKA TELKHLQCLE 60
 EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 145 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 145
 APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTYML TFKFYMPKKA TELKHLQCLE 60
 EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 146 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 146
 APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTVML TFKFYMPKKA TELKHLQCLE 60
 EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 147 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 147
 APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTAML TFKFYMPKKA TELKHLQCLE 60
 EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 148 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 148
 APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTQML TFKFYMPKKA TELKHLQCLE 60

-continued

EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 149 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 149
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 150 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 150
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTDML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 151 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 151
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFEFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 152 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 152
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
AELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 153 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 153
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EALKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 154 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 154
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EYLKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 155 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 155
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 156 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 156

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APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NHAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

```

```

SEQ ID NO: 157      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 157
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NRAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

```

```

SEQ ID NO: 158      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 158
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TDKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

```

```

SEQ ID NO: 159      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 159
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TRKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

```

```

SEQ ID NO: 160      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 160
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML THKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

```

```

SEQ ID NO: 161      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 161
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TAKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

```

```

SEQ ID NO: 162      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 162
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFEFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

```

```

SEQ ID NO: 163      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 163
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFRMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

```

```

SEQ ID NO: 164      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

```

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```

SEQUENCE: 164
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFKMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 165      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

SEQUENCE: 165
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EALKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 166      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

SEQUENCE: 166
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EYLKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 167      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

SEQUENCE: 167
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NDAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 168      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

SEQUENCE: 168
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NHAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 169      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

SEQUENCE: 169
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NRAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 170      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

SEQUENCE: 170
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTDML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 171      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

SEQUENCE: 171
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 172      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein

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                organism = Synthetic construct
SEQUENCE: 172
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTQML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 173      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                  mol_type = protein
                  organism = Synthetic construct

SEQUENCE: 173
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTAML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 174      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                  mol_type = protein
                  organism = Synthetic construct

SEQUENCE: 174
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISRIN VIVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 175      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                  mol_type = protein
                  organism = Synthetic construct

SEQUENCE: 175
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRRLISNIN VIVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 176      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                  mol_type = protein
                  organism = Synthetic construct

SEQUENCE: 176
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRKLISNIN VIVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 177      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                  mol_type = protein
                  organism = Synthetic construct

SEQUENCE: 177
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TAKFRMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 178      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                  mol_type = protein
                  organism = Synthetic construct

SEQUENCE: 178
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML THKFRMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 179      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                  mol_type = protein
                  organism = Synthetic construct

SEQUENCE: 179
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTDML TFKFYMPKKA TELKHLQCLE 60
RELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 180      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133

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mol_type = protein
organism = Synthetic construct
SEQUENCE: 180
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
RELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 181      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct
SEQUENCE: 181
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTQML TFKFYMPKKA TELKHLQCLE 60
RELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 182      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct
SEQUENCE: 182
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTAML TFKFYMPKKA TELKHLQCLE 60
RELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 183      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct
SEQUENCE: 183
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTAML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLALKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 184      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct
SEQUENCE: 184
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTDML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLALKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 185      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct
SEQUENCE: 185
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLALKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 186      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct
SEQUENCE: 186
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTQML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLALKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 187      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct
SEQUENCE: 187
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TRKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLALKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 188      moltype = AA length = 133
FEATURE            Location/Qualifiers

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source                1..133
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 188
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TAKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLALKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT                                             133

SEQ ID NO: 189        moltype = AA length = 133
FEATURE              Location/Qualifiers
source                1..133
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 189
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TDKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLALKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT                                             133

SEQ ID NO: 190        moltype = AA length = 133
FEATURE              Location/Qualifiers
source                1..133
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 190
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML THKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLALKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT                                             133

SEQ ID NO: 191        moltype = AA length = 133
FEATURE              Location/Qualifiers
source                1..133
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 191
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TKKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLALKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT                                             133

SEQ ID NO: 192        moltype = AA length = 133
FEATURE              Location/Qualifiers
source                1..133
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 192
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFAFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLALKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT                                             133

SEQ ID NO: 193        moltype = AA length = 133
FEATURE              Location/Qualifiers
source                1..133
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 193
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFEFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLALKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT                                             133

SEQ ID NO: 194        moltype = AA length = 133
FEATURE              Location/Qualifiers
source                1..133
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 194
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFQFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLALKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT                                             133

SEQ ID NO: 195        moltype = AA length = 133
FEATURE              Location/Qualifiers
source                1..133
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 195
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFAMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLALKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT                                             133

SEQ ID NO: 196        moltype = AA length = 133

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FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 196
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFKMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLALKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 197 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 197
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFSPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLALKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 198 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 198
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFRMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLALKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 199 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 199
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
AELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLALKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 200 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 200
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EALKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLALKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 201 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 201
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
ERLKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLALKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 202 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 202
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EKLKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLALKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 203 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 203
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EYLKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLALKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

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SEQ ID NO: 212 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 212
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLALKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 213 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 213
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TTKFRMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLIANIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 214 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 214
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TTKFRMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLALKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 215 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 215
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFAQSIIS TLT 133

SEQ ID NO: 216 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 216
APASSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 217 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 217
APASSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFAQSIIS TLT 133

SEQ ID NO: 218 moltype = AA length = 130
FEATURE Location/Qualifiers
source 1..130
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 218
SSSTKKTQLQ LEHLLLALQM ILNGINNYKN PKLTEMLTFK FYMPKKATEL KHLQCLEEEL 60
KPLEEVLNLA QSKNFHLRPR DLISNINVIV LELKGSETTF MCEYADETAT IVEFLNRWIT 120
FCQSIISTLT 130

SEQ ID NO: 219 moltype = AA length = 130
FEATURE Location/Qualifiers
source 1..130
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 219
SSSTKKTQLQ LEHLLLALQM ILNGINNYKN PKLTEMLTFK FYMPKKATEL KHLQCLEEEL 60
KPLEEVLNLA QSKNFHLRPR DLISNINVIV LELKGSETTF MCEYADETAT IVEFLNRWIT 120

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FAQSIISTLT 130
 SEQ ID NO: 220 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct
 SEQUENCE: 220
 APTSSSTKKT QLQLEHLLLD LAMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
 EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133
 SEQ ID NO: 221 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct
 SEQUENCE: 221
 APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
 EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WIAFCQSIIS TLT 133
 SEQ ID NO: 222 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct
 SEQUENCE: 222
 APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
 EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIAS TLT 133
 SEQ ID NO: 223 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct
 SEQUENCE: 223
 APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
 EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIA TLT 133
 SEQ ID NO: 224 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct
 SEQUENCE: 224
 APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
 EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCASIIS TLT 133
 SEQ ID NO: 225 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct
 SEQUENCE: 225
 APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
 EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCDSIIS TLT 133
 SEQ ID NO: 226 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct
 SEQUENCE: 226
 APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
 EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCVSIIS TLT 133
 SEQ ID NO: 227 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct
 SEQUENCE: 227
 APTSSSTKKT QLQLEHLLLD LAMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60

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EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIA TLT 133

SEQ ID NO: 228 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 228
APTSSSTKKT QLQLEHLLD LQMILNGINN YKNPKLTRML TTKFMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCDSIIS TLT 133

SEQ ID NO: 229 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 229
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLALKGSE TTFMCEYADE TATIVEFLNR 120
WITFCDSIIS TLT 133

SEQ ID NO: 230 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 230
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
RELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 231 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 231
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
NELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 232 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 232
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
DELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 233 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 233
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
QELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 234 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 234
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
GELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 235 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 235

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APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
HELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

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SEQ ID NO: 236      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 236
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
IELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

```

```

SEQ ID NO: 237      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 237
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
LELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

```

```

SEQ ID NO: 238      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 238
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
KELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

```

```

SEQ ID NO: 239      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 239
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
MELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

```

```

SEQ ID NO: 240      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 240
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
FELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

```

```

SEQ ID NO: 241      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 241
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
PELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

```

```

SEQ ID NO: 242      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 242
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
SELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

```

```

SEQ ID NO: 243      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

```

-continued

SEQUENCE: 243
 APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
 TELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 244 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 244
 APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
 WELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 245 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 245
 APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
 YELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 246 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 246
 APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
 VELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 247 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 247
 APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TNKFYMPKKA TELKHLQCLE 60
 EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 248 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 248
 APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TQKFYMPKKA TELKHLQCLE 60
 EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 249 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 249
 APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TEKFYMPKKA TELKHLQCLE 60
 EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 250 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 250
 APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TGKFYMPKKA TELKHLQCLE 60
 EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 251 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein

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                                organism = Synthetic construct
SEQUENCE: 251
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TIKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 252      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

SEQUENCE: 252
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TLKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 253      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

SEQUENCE: 253
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TMKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 254      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

SEQUENCE: 254
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TPKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 255      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

SEQUENCE: 255
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TSKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 256      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

SEQUENCE: 256
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TTKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 257      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

SEQUENCE: 257
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TWKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 258      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

SEQUENCE: 258
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TYKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 259      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133

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mol_type = protein
organism = Synthetic construct
SEQUENCE: 259
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TVKPYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 260      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct
SEQUENCE: 260
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFAMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 261      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct
SEQUENCE: 261
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFNMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 262      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct
SEQUENCE: 262
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFDPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 263      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct
SEQUENCE: 263
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFQMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 264      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct
SEQUENCE: 264
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFEMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 265      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct
SEQUENCE: 265
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 266      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct
SEQUENCE: 266
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFHMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 267      moltype = AA length = 133
FEATURE           Location/Qualifiers

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source                1..133
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 267
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFIMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT                                             133

SEQ ID NO: 268        moltype = AA length = 133
FEATURE              Location/Qualifiers
source               1..133
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 268
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFLMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT                                             133

SEQ ID NO: 269        moltype = AA length = 133
FEATURE              Location/Qualifiers
source               1..133
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 269
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT                                             133

SEQ ID NO: 270        moltype = AA length = 133
FEATURE              Location/Qualifiers
source               1..133
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 270
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFFMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT                                             133

SEQ ID NO: 271        moltype = AA length = 133
FEATURE              Location/Qualifiers
source               1..133
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 271
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT                                             133

SEQ ID NO: 272        moltype = AA length = 133
FEATURE              Location/Qualifiers
source               1..133
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 272
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFSMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT                                             133

SEQ ID NO: 273        moltype = AA length = 133
FEATURE              Location/Qualifiers
source               1..133
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 273
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFTMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT                                             133

SEQ ID NO: 274        moltype = AA length = 133
FEATURE              Location/Qualifiers
source               1..133
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 274
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFWMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT                                             133

SEQ ID NO: 275        moltype = AA length = 133

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FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 275
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTRML TFKFVMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 276 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 276
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TNKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 277 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 277
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TQKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 278 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 278
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TEKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 279 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 279
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TGKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 280 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 280
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TIKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 281 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 281
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TLKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 282 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
mol_type = protein
organism = Synthetic construct

SEQUENCE: 282
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TKKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

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SEQ ID NO: 291 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 291
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFNMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 292 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 292
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFDMPPKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 293 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 293
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFQMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 294 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 294
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFEMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 295 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 295
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFGMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 296 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 296
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFHMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 297 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 297
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFIMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 298 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 298
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFLMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120

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WITFCQSIIS TLT 133

SEQ ID NO: 299 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 299
 APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFMPKKA TELKHLQCLE 60
 EELKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 300 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 300
 APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFMPKKA TELKHLQCLE 60
 EELKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 301 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 301
 APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFMPKKA TELKHLQCLE 60
 EELKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 302 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 302
 APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFMPKKA TELKHLQCLE 60
 EELKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 303 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 303
 APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFTMPKKA TELKHLQCLE 60
 EELKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 304 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 304
 APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFWMPKKA TELKHLQCLE 60
 EELKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 305 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 305
 APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFVMPKKA TELKHLQCLE 60
 EELKPLEEVL NLAQSKNFHL RPRDLISNIN VDVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 306 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 306
 APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60

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EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 307 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 307
APTSSSTKKT QLQLEHLLLS LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 308 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 308
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TAKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISRIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 309 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 309
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TAKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISDIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 310 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 310
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRALISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 311 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 311
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRNLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 312 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 312
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRQLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 313 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 313
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRELISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 314 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 314

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APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRGLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

```

```

SEQ ID NO: 315      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 315
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRHLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

```

```

SEQ ID NO: 316      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 316
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRILISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

```

```

SEQ ID NO: 317      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 317
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRLLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

```

```

SEQ ID NO: 318      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 318
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRMLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

```

```

SEQ ID NO: 319      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 319
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRFLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

```

```

SEQ ID NO: 320      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 320
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRPLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

```

```

SEQ ID NO: 321      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 321
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRSLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

```

```

SEQ ID NO: 322      moltype = AA length = 133
FEATURE            Location/Qualifiers
source             1..133
                   mol_type = protein
                   organism = Synthetic construct

```

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SEQUENCE: 322
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRTLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 323 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 323
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRWLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 324 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 324
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRYLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 325 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 325
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRVLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 326 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 326
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VAVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 327 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 327
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VRVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 328 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 328
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VNVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 329 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 329
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VQVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 330 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein

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                                organism = Synthetic construct
SEQUENCE: 330
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VEVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 331      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct

SEQUENCE: 331
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VGVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 332      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct

SEQUENCE: 332
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VHVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 333      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct

SEQUENCE: 333
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VLVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 334      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct

SEQUENCE: 334
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VKVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 335      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct

SEQUENCE: 335
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VMVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 336      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct

SEQUENCE: 336
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 337      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct

SEQUENCE: 337
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VVLELKGSE TTFMCEYADE TATIVEEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 338      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133

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mol_type = protein
organism = Synthetic construct
SEQUENCE: 338
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VSVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 339      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct
SEQUENCE: 339
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VTVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 340      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct
SEQUENCE: 340
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 341      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct
SEQUENCE: 341
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 342      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct
SEQUENCE: 342
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 343      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct
SEQUENCE: 343
APTSSSTKKT QLQLEELLDD LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 344      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct
SEQUENCE: 344
APTSSSTKKT QLQLEHLLLA LQMILNGINN YKNPKLTKML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 345      moltype = AA length = 133
FEATURE           Location/Qualifiers
source           1..133
                 mol_type = protein
                 organism = Synthetic construct
SEQUENCE: 345
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 346      moltype = AA length = 268
FEATURE           Location/Qualifiers

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source                1..268
                    mol_type = protein
                    organism = Synthetic construct

SEQUENCE: 346
PGWFLDSPDR PWNPPTFSPA LLVVTEGDNA TFTCSFSNTS ESFVLNWYRM SPSNQTDKLA 60
AFPEDRSQPG QDCRFRTQL PNGRDFHMSV VRARRNDSGT YLCGAILSLAP KAQIKESLRA 120
ELRVTERRAE VPTAHPSPSP RPAGQFQTLV VGVVGLLGS LVLLVWVLAV ICSRAARGTI 180
GARRTGQPLK EDPASAVVFS VDYGELDFQW REKTPPEPPVP CVPEQTEYAT IVFPPSGMGTS 240
SPARRGSADG PRSAQPLRPE DGHCSWPL 268

SEQ ID NO: 347      moltype = DNA length = 804
FEATURE            Location/Qualifiers
source             1..804
                    mol_type = other DNA
                    organism = Synthetic construct

SEQUENCE: 347
ccagatggt tcttagactc cccagacagg ccttgaacc cccccacct ctccccagcc 60
ctgctcgtgg tgaccgaagg ggacaacgcc accttcacct gcagcttctc caacacatcg 120
gagagcttgc tgactaaact gtaccgcatg agccccagca accagacgga caagctggcc 180
gccttccccg aggaccgcag ccagcccgcc caggactgcc gcttcctgtg cacacaactg 240
cccaacgggc gtgacttcca catgagcgtg gtcaggggccc ggcgcaatga cagcggcacc 300
tacctctgtg gggccatctc cctggccccc aaggcgcaga tcaaagagag cctgcgggca 360
gagctcaggg tgacagagag aagggcagaa gtgcccacag cccaccccag cccctcacc 420
aggccagccg gccagttcca aacctgggtg gttggtgctg tggcggcct gctgggcagc 480
ctggtgctgc tagtctgggt cctggccgctc atctgctccc gggccgcacg agggacaata 540
ggagccaggg gcaccggcca gccccctgaag gaggaccctc cagccctgcc tgtgtctct 600
gtggactatg gggagctgga tttccagtg cagagagaaga ccccgagcc ccccgctgcc 660
tgtgtccctg agcagacgga gtagccacc attgtcttc ctagcgggat gggcacctca 720
tccccgccc gcaggggctc agctgacggc cctcggagtg cccagccact gaggcctgag 780
gatggacact gctcttgccc cctc 804

SEQ ID NO: 348      moltype = AA length = 449
FEATURE            Location/Qualifiers
source             1..449
                    mol_type = protein
                    organism = Synthetic construct

SEQUENCE: 348
QVQLVESGGG VVQGRSLRL DCKASGITFS NSGMHWVRQA PGKGLEWVAV IWYDGSKRY 60
ADSVKGRFTI SRDNSKNTLF LQMNSLRAED TAVYYCATND DYWGQGLT VSSAKTTPPS 120
VYPLAPGCGD TTGSSVTLGC LVKGYFPESV TVTWNSGSLG SSVHTFPALL QSGLYTMSSS 180
VTVPSSTWPS QTVTCSVAHP ASSTTVDKKL EPSGPISTIN PCPPCKECKH CPAPNLEGGP 240
SVFI FPPNIK DVLMLISLTPK VTCVVVDVSE DDPDVQISWF VNNVEVHTAQ TQTHREDYAS 300
TIRVSVTLPI QHQDWMGKKE FKCKVNNKDL PSPIERTISK IKGLVRAPQV YILPPPAEQ 360
SRKDVSLTCL VVGFNPGDIS VEWTNSNGHTE ENYKDTAPVL DSDGSYFIYS KLNMKTSKWE 420
KTDSFSCNVR HEGLKNYYLK KTISRSPGK 449

SEQ ID NO: 349      moltype = AA length = 214
FEATURE            Location/Qualifiers
source             1..214
                    mol_type = protein
                    organism = Synthetic construct

SEQUENCE: 349
EIVLTQSPAT LSLSPGERAT LSCRASQSVS SYLAWYQQKP GQAPRLLIYD ASNRATGIPA 60
RFSGSGSGTD FTLTISLLEP EDFAVYYCQQ SSNWPRTPGQ GTKVEIKRAD AAPTIVSIFPP 120
SSEQLTSGGA SVVCFLNIFY PKDINVKWKI DGSERQNGVL NSWTDQDSKD STYSMSSTLT 180
LTKDEYERHN SYTCEATHKT STSPIVKSFN RNEC 214

SEQ ID NO: 350      moltype = AA length = 456
FEATURE            Location/Qualifiers
source             1..456
                    mol_type = protein
                    organism = Synthetic construct

SEQUENCE: 350
QVQLVQSGVE VKKPGASVKV SCKASGYTFT NYYMYWVRQA PGQGLEWVGG INPSNGGTNF 60
NEKFKNRVTL TTDSTTTAY MELKSLQFDD TAVYYCARRD YRFDMGFQYV GQGTIVTVSS 120
AKTTPPSVYP LAPGCGDITG SSVTLGCLVK GYFPESVTVT WNSGSLSSV HTPFALLQSG 180
LYTMSSSVTV PSSVWPSQTV TCSVAHPASS TVDKKLEPS GPISTINPCP PCKECKCPA 240
PNLEGGPSVF IFPPNIKDVL MISLTPKVT C VVDVSEDDP DVQISWVFN VEVHTAQQT 300
HREDYASTIR VVSTLPIQHQ DWMGKKEFKC KVNKDLPSI IERTISKIKG LVRAPQVYIL 360
PPPAPQLSRK DVSLTCLVVG FNPGLDISVEW TSNHTEENY KDTAPVLDSG GSYFIYSKLN 420
MKTSKWEKTD SFSCNVRHEG LKNYYLKKTI SRSPGK 456

SEQ ID NO: 351      moltype = AA length = 218
FEATURE            Location/Qualifiers
source             1..218
                    mol_type = protein
                    organism = Synthetic construct

SEQUENCE: 351
EIVLTQSPAT LSLSPGERAT LSCRASKGVS TSGSYLHWY QKPKGQAPRL LIYLASYLES 60

```

-continued

| | | | | | | |
|------------|------------|------------|------------|------------|------------|-----|
| GVPARFSGSG | SGTDFTLTIS | SLEPEDFAVY | YCQHSRDLP | TFGGGTKVEI | KRADAAPT | 120 |
| IFPPSSEQLT | SGGASVVCFL | NNFYPKDINV | KWKIDGSEKQ | NGVLNSWTDQ | DSKDSTYSMS | 180 |
| STLTLTKDEY | ERHNSYTCEA | THKTSTSPIV | KSFNRNEC | | | 218 |

SEQ ID NO: 352 moltype = AA length = 347
 FEATURE Location/Qualifiers
 source 1..347
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 352

| | | | | | | |
|------------|------------|------------|------------|------------|------------|-----|
| LNTTILTPNG | NEDTTADFFL | TTMPTDLSLV | STLPLPEVQC | FVFNVEYMNC | TWNSSEPPQ | 60 |
| TNLTLHYWYK | NSDNDKVQKC | SHYLFSEIEI | SGCQLQKKEI | HLYQTFVVQL | QDPRPRRQA | 120 |
| TQMLKLQNLV | IPWAPENLTL | HKLSESQLEL | NWNNRFLNHC | LEHLVQYRTD | WDHSWTEQSV | 180 |
| DYRHKFSLPS | VDGQKRYTFR | VRSRFPNPLC | SAQHWSEWSH | PIHWSNNTSK | ENPFPLALEA | 240 |
| VVISVGSMLG | IISLLCVYFW | LERTMPRIPT | LKNLEDLVTE | YHGNFSAWSG | VSKGLAESLQ | 300 |
| PDYSERLCLV | SEIPPKGGAL | GEGPGASPCN | QHSFYWAPP | YTLKPET | | 347 |

SEQ ID NO: 353 moltype = AA length = 525
 FEATURE Location/Qualifiers
 source 1..525
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 353

| | | | | | | |
|-------------|-------------|------------|------------|------------|------------|-----|
| AVNGTSQPTC | FYNSTRANISC | VWSQDQALQD | TSCQVHAWPD | RRRWNQTC | LPVSQASWAC | 60 |
| NLILGAPDSQ | KLTTVDIVTL | RVLCREGVRV | RVMAIQDFKP | FENLRMLAPI | SLQVHVHETH | 120 |
| RCNISWEISQ | ASHYFERHLE | FEARTLSPGH | TWEEAPLLTL | KKQKEWICLE | TLTPDTQYEF | 180 |
| QVRVKPLQGE | FTTWSPWSQP | LAFRTKPAAL | GKDTIPWLGH | LLVGLSGAFG | FIIIVYLLIN | 240 |
| CRNTGPWLKK | VLKCNTPDPS | KFFSQLSSEH | GGDVQKWLSS | PFPSSSSPG | GLAPEISPLE | 300 |
| VLERDKVTQL | LLQDQKVEPE | ASLSSNHSLT | SCFTNQGYFF | PHLPDALEIE | ACQVYFTYDP | 360 |
| YSEEDPDEGV | AGAPTGSQP | PLQPLSGEDD | AYCTFPPSRD | LLLFPSPLLG | GPSPPSTAPG | 420 |
| GSAGAGEERMP | PSLQERVPRD | WDQPLGPPT | PGVPLVDVDF | PPPELVLEA | GEEVPDAGPR | 480 |
| EGVSPWSPRP | PGQGEFRALN | ARLPLNTDAY | LSQLQLQGD | PTHLV | | 525 |

SEQ ID NO: 354 moltype = AA length = 251
 FEATURE Location/Qualifiers
 source 1..251
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 354

| | | | | | | |
|------------|------------|------------|------------|------------|------------|-----|
| ELCDDDPPEI | PHATFKAMAY | KEGTMLNCEC | KRGFRRIKSG | SLYMLCTGNS | SHSSWDNQCC | 60 |
| CTSSATRNTT | KQVTPQPEEQ | KERKTTEMQS | PMQPVDAQSL | PGHCREPPPW | ENEATERIYH | 120 |
| FVVGQMVYYQ | CVQGYRALHR | GPAESVCKMT | HGKTRWTQPQ | LICTGEMETS | QPPGEEKPQA | 180 |
| SPEGRPESET | SCLVTTDFQ | IQTEMAATME | TSIFTFEYQV | AVAGCVFLLI | SVLLLSGLTW | 240 |
| QRRQRKSRR | I | | | | | 251 |

SEQ ID NO: 355 moltype = AA length = 6
 FEATURE Location/Qualifiers
 source 1..6
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 355

| | | | | | | |
|--------|--|--|--|--|--|---|
| SGGGGS | | | | | | 6 |
|--------|--|--|--|--|--|---|

SEQ ID NO: 356 moltype = AA length = 346
 FEATURE Location/Qualifiers
 source 1..346
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 356

| | | | | | | |
|------------|------------|------------|------------|-------------|------------|-----|
| APTSSSTKKT | QLQLEHLLLD | LQMILNGINN | YKNPKLTRML | TFKPYMPKKA | TELKHLQCLE | 60 |
| EELKPLEEVL | NLAQSKNFHL | RPRDLISNIN | VIVLELKGSE | TFMCEYADE | TATIVEFLNR | 120 |
| WITFCQSIIS | TLTDTVLTQS | PALAVSPGER | VTISCRASES | VRTGVHWHYQQ | KPGQQPKLLI | 180 |
| YGASNLESGV | PARFSGSGSG | TDFTLTIDPV | EADDTATYFC | QOSWNPPTF | GSQTKLEIKR | 240 |
| TVAAPSVFIF | PPSDEQLKSG | TASVVCLLNN | FYPREAKVQW | KVDNALQSGN | SQESVTEQDS | 300 |
| KDSTYSLSST | LTLKADYK | HKVYACEVTH | QGLSSPVTKS | FNRGEC | | 346 |

SEQ ID NO: 357 moltype = AA length = 352
 FEATURE Location/Qualifiers
 source 1..352
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 357

| | | | | | | |
|------------|------------|------------|------------|------------|-------------|-----|
| APTSSSTKKT | QLQLEHLLLD | LQMILNGINN | YKNPKLTRML | TFKPYMPKKA | TELKHLQCLE | 60 |
| EELKPLEEVL | NLAQSKNFHL | RPRDLISNIN | VIVLELKGSE | TFMCEYADE | TATIVEFLNR | 120 |
| WITFCQSIIS | TLTSGGGGSD | TVLTQSPALA | VSPGERVTIS | CRASESVRTG | VHWHYQQKPGQ | 180 |
| QKLLIYGAS | NLESGVPARF | SGSGSGTDF | LTIDPVEADD | TATYFCQOSW | NDPPTFGSGT | 240 |
| KLEIKRTVAA | PSVFIFPPSD | EQLKSGTASV | VCLLNNFYPR | EAKVQWKVDN | ALQSGNSQES | 300 |
| VTEQDSKST | YLSSTLTL | KADYKHKVY | ACEVTHQGLS | SPVTKSPNRG | EC | 352 |

-continued

```

SEQ ID NO: 358      moltype = AA length = 580
FEATURE            Location/Qualifiers
source             1..580
                  mol_type = protein
                  organism = Synthetic construct

SEQUENCE: 358
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLTEVQLVES GGGVLVQGRS LKLSCAVSGF TFSDYAMAWV RQAPKKGLEW 180
VATISYDGSR TYYRDSVYGR FTISRDNAKI TLYLQMDSLR SEDTATYYCA RHGSGYFDYW 240
GQGVMTVSS ASTKGPSVFP LAPSSKSTSG GTAALGCLVK DYFPEPVTVS WNSGALTSKV 300
HTFPAVLQSS GLYSLSSVVT VPSSSLGTQT YICNVNPKPS NTKVDKKEVP KSCDKTHTCP 360
PCPAPELLGG PSVFLFPPKP KDTLMISRTP EVTCVVVDVS HEDPEVKFNW YVDGVEVHNA 420
KTKPREEQYN STYRVVSVLT VLHQDWLNGK EYKCKVSNKA LPAPIEKTIS KAKGQPREPQ 480
VYTLPPSRDE LTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTTPV LDSDGSFFLY 540
SKLTVDKSRW QQGNVFCSSV MHEALHNHYT QKSLSLSPGK 580

SEQ ID NO: 359      moltype = AA length = 586
FEATURE            Location/Qualifiers
source             1..586
                  mol_type = protein
                  organism = Synthetic construct

SEQUENCE: 359
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLTSGGGGSE VQLVESGGGL VQPGRSLKLS CAVSGFTFSD YAMAWVRQAP 180
KKGLEWVATI SYDGSRTYYR DSVKGRFTIS RDNAKITLYL QMDSLRS EDT ATYYCARHGS 240
GYFDYWGQGV MVTVSSASTK GPSVFLPLAPS SKSTSGGTAA LGCLVKDYFP EPVTVSWNSG 300
ALTSVHTFP AVLQSSGLYS LSSVVTVPSS SLGTQTYICN VNHKPSNTKV DKKVEPKSCD 360
KTHTCPPEPA PELLGGPSVF LPPPKPKDTL MISRTPEVTC VVVDVSHEDP EVKFNWYVDG 420
VEVHNAKTKP REEQYNSTYR VVSVLTVLHQ DWLNGKEYK KVSNKALPA IEKTISKAKG 480
QPREPQVYTL PPSRDELTKN QVSLTCLVKG FYPVDIAVEW ESNQGPENNY KTTTPVLDS 540
GSFFLYSKLT VDKSRWQQGN VFCSSVMHEA LHNHYTQKSL SLSPGK 586

SEQ ID NO: 360      moltype = AA length = 580
FEATURE            Location/Qualifiers
source             1..580
                  mol_type = protein
                  organism = Synthetic construct

SEQUENCE: 360
EVQLVESGGG LVQPGRSLKL SCAVSGFTFS DYAMAWVRQA PPKGLEWVAT ISYDGSRTYY 60
RDSVKGRFTI SRDNAKITLY LQMDLSRSED TATYYCARHG SGYFDYWGQG VMVTVSSAST 120
KGPSVFLPLAP SSKSTSGGTA ALGCLVKDYF PEPVTVSWNS GALTSGVHTF PAVLQSSGLY 180
SLSSVVTVPS SSLGTQTYIC NVNHKPSNTK VDKKVEPKSC DKHTHTCPPCP APELLGGPSV 240
FLFPPKPKDT LMSRTPPEVT CVVVDVSHED PEVKFNWYVD GVEVHNAKTK PREEQYNSTY 300
RVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK GQPREPQVYT LPPSRDELTK 360
NQVSLTCLVK GFYPSDIAVE WESNGQPENNY YKTTTPVLDS DGSFFLYSKL TVDKSRWQQG 420
NVFSCVMHE ALHNHYTQKS LSLSPGKAPT SSSSTKKTQLQ LEHLLLDLQM ILNGINNYKN 480
PKLTRMLTFK FYMPKATEL KHLQCLEEEL KPLEEVLNLA QSKNFHLRPR DLISNINIVIV 540
LELKGSETTF MCEYADETAT IVEFLNRWIT FCQSIISTLT 580

SEQ ID NO: 361      moltype = AA length = 586
FEATURE            Location/Qualifiers
source             1..586
                  mol_type = protein
                  organism = Synthetic construct

SEQUENCE: 361
EVQLVESGGG LVQPGRSLKL SCAVSGFTFS DYAMAWVRQA PPKGLEWVAT ISYDGSRTYY 60
RDSVKGRFTI SRDNAKITLY LQMDLSRSED TATYYCARHG SGYFDYWGQG VMVTVSSAST 120
KGPSVFLPLAP SSKSTSGGTA ALGCLVKDYF PEPVTVSWNS GALTSGVHTF PAVLQSSGLY 180
SLSSVVTVPS SSLGTQTYIC NVNHKPSNTK VDKKVEPKSC DKHTHTCPPCP APELLGGPSV 240
FLFPPKPKDT LMSRTPPEVT CVVVDVSHED PEVKFNWYVD GVEVHNAKTK PREEQYNSTY 300
RVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK GQPREPQVYT LPPSRDELTK 360
NQVSLTCLVK GFYPSDIAVE WESNGQPENNY YKTTTPVLDS DGSFFLYSKL TVDKSRWQQG 420
NVFSCVMHE ALHNHYTQKS LSLSPGKSGG GGSAPTSST KKTQLQLEHL LLDLQMLNG 480
INNYKNPKLT RMLTFKPYMP KKATELKHQ CLEELKPLE EVLNLAQSKN FHLRPRDLIS 540
NINIVLELK GSETTFMCEY ADETATIVEF LNRWITFCQS IISTLT 586

SEQ ID NO: 362      moltype = AA length = 346
FEATURE            Location/Qualifiers
source             1..346
                  mol_type = protein
                  organism = Synthetic construct

SEQUENCE: 362
DTVLTQSPAL AVSPGERVTI SCRASESVRT GVHWYQQKPG QPKLLIYGA SNLESGVPA 60
FSGSGSGTDF TLTIDPVEAD DTATYFCQQS WNDPFTFGSG TKLEIKRTVA APSVFIFPPS 120
DEQLKSGTAS VVCLLNNFYP REAKVQWKVD NALQSGNSQE SVTEQDSKDS TYSLSSTLTL 180
SKADYEKHKV YACEVTHQGL SSPVTKSFNR GECAPTSST KKTQLQLEHL LLDLQMLNG 240
INNYKNPKLT RMLTFKPYMP KKATELKHQ CLEELKPLE EVLNLAQSKN FHLRPRDLIS 300

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NINVIVLELK GSETTFMCEY ADETATIVEF LNRWITFCQS IISTLT 346

SEQ ID NO: 363 moltype = AA length = 352
 FEATURE Location/Qualifiers
 source 1..352
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 363
 DTVLTQSPAL AVSPGERVTI SCRAESVRT GVHWYQQKPG QPKLLIYGA SNLESGVVPAR 60
 FSGSGSGTDF TLTIDPVEAD DTATYPCQQS WNDPPTFGSG TKLEIKRTVA APSVFIIPPS 120
 DEQLKSGTAS VVCLLNFFYP REAKVQWKVD NALQSGNSQE SVTEQDSKDS TYSLSSTLTL 180
 SKADYEKHKV YACEVTHQGL SSPVTKSFNR GECSGGGSA PTSSSTKKTQ LQLEHLLLDL 240
 QMLNGINNY KNPRLRMLT FKFYMPKKAT ELKHLQCLEE ELKPLEEVLN LAQSKNFHLR 300
 PRDLISINIV IVLELKGSET TFMCEYADET ATIVEFLNRW ITFCQSIIST LT 352

SEQ ID NO: 364 moltype = AA length = 20
 FEATURE Location/Qualifiers
 source 1..20
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 364
 SGGGSGGGG SGGGSGGGG 20

SEQ ID NO: 365 moltype = AA length = 764
 FEATURE Location/Qualifiers
 source 1..764
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 365
 ELCDDDPPEI PHATFKAMAY KEGTMLNCEC KRGFRRIKSG SLYMLCTGNS SHSSWDNQCQ 60
 CTSSATRNTT KQVTPQPEEQ KERKTEMQS PMQPVDQASL PGHCREPPPW ENEATERIYH 120
 FVVGQMVYYQ CVQGYRALHR GPAESVCKMT HGKTRWTQPQ LICITSGGGGS GGGGSGGGGS 180
 GGGSAPTSSS TKKTQLQLEH LLLDLQMI LN GINNYKNPKL TRMLTFKPYM PKKATELKLH 240
 QCLEEELKPL EEVLNLAQSK NFHLRPRDLI SNINVIVLEL KGETTFMCE YADETATIVE 300
 FLNRWITFCQ SIIISTLTVQ LVESGGGLVQ PGRSLKLSA VSGFTFSDYA MAWVRQAPKK 360
 GLEWVATISY DGSRTYRDS VKGRFTISR NAKITLYLQM DSLRSEDAT YYCARHSGSY 420
 FDYWGQVMV TVSSASTKGP SVFPLAPSSK STSGGTAALG CLVKDYFPEP VTVSWNSGAL 480
 TSGVHTFPAV LQSSGLYSL SVVTVPSSSL GTQTYICNVN HKPSNTKVDK KVEPKSCDKT 540
 HTCPCPAPPE LLGGPSVFLF PPKPKDTLMI SRTPEVTCVV VDVSHEDPEV KFNWYVDGVE 600
 VHNAKTKPRE EQYNSTYRVV SVLTVLHQDW LNGKEYKCKV SNKALPAPIE KTIKAKGQP 660
 REPQVYTLPP SRDELTKNQV SLTCLVKGFY PSDIAVEWES NGQPENNYKT TPPVLDSGGS 720
 PFLYSKLTVD KSRWQQGNVF SCSVMHEALH NHYTQKSLSL SPGK 764

SEQ ID NO: 366 moltype = AA length = 770
 FEATURE Location/Qualifiers
 source 1..770
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 366
 ELCDDDPPEI PHATFKAMAY KEGTMLNCEC KRGFRRIKSG SLYMLCTGNS SHSSWDNQCQ 60
 CTSSATRNTT KQVTPQPEEQ KERKTEMQS PMQPVDQASL PGHCREPPPW ENEATERIYH 120
 FVVGQMVYYQ CVQGYRALHR GPAESVCKMT HGKTRWTQPQ LICITSGGGGS GGGGSGGGGS 180
 GGGSAPTSSS TKKTQLQLEH LLLDLQMI LN GINNYKNPKL TRMLTFKPYM PKKATELKLH 240
 QCLEEELKPL EEVLNLAQSK NFHLRPRDLI SNINVIVLEL KGETTFMCE YADETATIVE 300
 FLNRWITFCQ SIIISTLTSGG GGSEVQLVES GGGLVQPGRS LKLSCAVSGF TFSYAMAWV 360
 RQAPKKGLEW VATISYDGR TYRDSVKGR FTISRDNKI TLYLQMDSLR SEDTATYYCA 420
 RHGSGFYDYG GQGMVTVSS ASTKGPSVFP LAPSSKSTSG GAAALGLVKV DYFPEPVTVS 480
 WNSGALTSGV HTPPAVLQSS GLYSLSSVVT VPSSSLGTQT YICNVNHKPS NTKVDKKEP 540
 KSCDKHTTCP PCPAPPELLG PSVFLFPPPK KDTLMISRTP EVTCVVVDVS HEDPEVKFNW 600
 YVDGVEVHNA KTKPREQYN STYRVVSVLT VLHQDWLNGK EYKCKVSNKA LPAPIEKTIS 660
 KAKGQPREPQ VYTLPPSRDE LTKNQVSLT LKGFYPSDI AVEWESNGQP ENNYKTTTPV 720
 LDSGSGFFLY SKLTVDKSRW QQGNVFSCSV MHEALHNYHT QKSLSLSPGK 770

SEQ ID NO: 367 moltype = AA length = 530
 FEATURE Location/Qualifiers
 source 1..530
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 367
 ELCDDDPPEI PHATFKAMAY KEGTMLNCEC KRGFRRIKSG SLYMLCTGNS SHSSWDNQCQ 60
 CTSSATRNTT KQVTPQPEEQ KERKTEMQS PMQPVDQASL PGHCREPPPW ENEATERIYH 120
 FVVGQMVYYQ CVQGYRALHR GPAESVCKMT HGKTRWTQPQ LICITSGGGGS GGGGSGGGGS 180
 GGGSAPTSSS TKKTQLQLEH LLLDLQMI LN GINNYKNPKL TRMLTFKPYM PKKATELKLH 240
 QCLEEELKPL EEVLNLAQSK NFHLRPRDLI SNINVIVLEL KGETTFMCE YADETATIVE 300
 FLNRWITFCQ SIIISTLTDV LTQSPALAVS PGERVTISCR ASESVRTGVH WYQQKPGQQP 360
 KLLIYGASNL ESGVPAFSG SSGSDFTFLT IDPVEADDTA TYFCQQSWND PFTFGSGTKL 420
 EIKRTVAAPS VFIFPPSDEQ LKSGTASVVC LLNMFYPREA KVQWKVDNAL QSGNSQESVT 480
 EQDSKSDTYS LSSLTLSLSKA DYEKHKVYAC EVTHQGLSSP VTKSFNRGEC 530

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SEQ ID NO: 368 moltype = AA length = 536
FEATURE Location/Qualifiers
source 1..536
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 368

| | | | | | | |
|------------|------------|-------------|------------|------------|------------|-----|
| ELCDDDPPEI | PHATFKAMAY | KEGTM LNCEC | KRGFRRIKSG | SLYMLCTGNS | SHSSWDNQCQ | 60 |
| CTSSATRNTT | KQVTPQPEEQ | KERKTTEMQS | PMQPVDAQSL | PGHCREPPPW | ENEATERIYH | 120 |
| FVVGQMVVYQ | CVQGYRALHR | GPAESVCKMT | HGKTRWTQPQ | LICTSGGGGS | GGGGSGGGGS | 180 |
| GGGSAPTSSS | TKKTQLQLEH | LLDLQMLN | GINNYKNPKL | TRMLTFKFYM | PKKATELKH | 240 |
| QCLEEELKPL | EEVLNLAQSK | NPHLRPRDLI | SNINVIVLEL | KGSETTFMCE | YADETATIVE | 300 |
| FLNRWITFCQ | SIISTLTSGG | GGSDTVLTQS | PALAVSPGER | VTISCRASES | VRTGVHWYQQ | 360 |
| KPGQQPKLLI | YGASNLESGV | PARFSGSGSG | TDFTLTIDPV | EADDTATYFC | QQSWNDPFTF | 420 |
| GSGTKLEIKR | TVAAPSVFIF | PPSDEQLKSG | TASVVCLLMN | FYPREAKVQW | KVDNALQSGN | 480 |
| SQESVTEQDS | KDSTYLSLST | LTLISKADYEK | HKVYACEVTH | QGLSSPVTKS | FNRGEC | 536 |

SEQ ID NO: 369 moltype = AA length = 764
FEATURE Location/Qualifiers
source 1..764
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 369

| | | | | | | |
|------------|------------|------------|------------|------------|--------------|-----|
| EVQLVESGGG | LVQPGRSLKL | SCAVSGFTFS | DYAMAWVRQA | PKKGLEWVAT | ISYDGSRTYY | 60 |
| RDSVKGRFTI | SRDNAKITLY | LQMDSLRSED | TATYYCARHG | SGYFDYWGQG | VMVTVSSAST | 120 |
| KGPSVFPPLA | SSKSTSGGTA | ALGCLVKDYF | PEPVTVSWNS | GALTSGVHTF | PAVLQSSGLY | 180 |
| SLSSVVTVPS | SSLGTQTYIC | NVNHKPSNTK | VDKKVEPKSC | DKTHTCPPCP | APELLGGPSV | 240 |
| FLFPPKPKDT | LMISRTPEVT | CVVVDVSHED | PEVKFNWYVD | GVEVHNAKTK | PREEQYNSTY | 300 |
| RVSVLTVLH | QDWLNGKEYK | CKVSNKALPA | PIEKTISKAK | GQPREPQVYT | LPPSRDELTK | 360 |
| NQVSLTCLVK | GFYPSDIAVE | WESNGQPENN | YKTTTPVLDS | DGSFFLYSKL | TVDKSRWQQG | 420 |
| NVFSQSVMHE | ALHNHYTQKS | LSLSPGKELC | DDDPEIIPHA | TFKAMAYKEG | TMLNCECKRG | 480 |
| FRRIKSGSLY | MLCTGNSSHS | SWDNQCQCTS | SATRNTTKQV | TPQPEEQKER | KTTEMQSPMQ | 540 |
| PVDQASLPGH | CREPPWENE | ATERIYHFVV | GQMVVYQCQV | GYRALHRGPA | ESVCKMTHGK | 600 |
| TRWTQPQLIC | TSGGGSGGGG | GSGGGSGGGG | SAPTSSTTKK | TQLQLEHLLL | DLQMI LINGIN | 660 |
| NYKNPKLTRM | LTFKPYMPKK | ATELKHQLCL | EEELKPLEEV | LNLAQSKNFH | LRPRDLISNI | 720 |
| NVIVLELKGK | ETTFMCEYAD | ETATIVEFLN | RWITFCQSII | STLT | | 764 |

SEQ ID NO: 370 moltype = AA length = 770
FEATURE Location/Qualifiers
source 1..770
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 370

| | | | | | | |
|-------------|------------|------------|------------|------------|-------------|-----|
| EVQLVESGGG | LVQPGRSLKL | SCAVSGFTFS | DYAMAWVRQA | PKKGLEWVAT | ISYDGSRTYY | 60 |
| RDSVKGRFTI | SRDNAKITLY | LQMDSLRSED | TATYYCARHG | SGYFDYWGQG | VMVTVSSAST | 120 |
| KGPSVFPPLA | SSKSTSGGTA | ALGCLVKDYF | PEPVTVSWNS | GALTSGVHTF | PAVLQSSGLY | 180 |
| SLSSVVTVPS | SSLGTQTYIC | NVNHKPSNTK | VDKKVEPKSC | DKTHTCPPCP | APELLGGPSV | 240 |
| FLFPPKPKDT | LMISRTPEVT | CVVVDVSHED | PEVKFNWYVD | GVEVHNAKTK | PREEQYNSTY | 300 |
| RVSVLTVLH | QDWLNGKEYK | CKVSNKALPA | PIEKTISKAK | GQPREPQVYT | LPPSRDELTK | 360 |
| NQVSLTCLVK | GFYPSDIAVE | WESNGQPENN | YKTTTPVLDS | DGSFFLYSKL | TVDKSRWQQG | 420 |
| NVFSQSVMHE | ALHNHYTQKS | LSLSPGKSGG | GGSELCDDDP | PEIPHATFKA | MAYKEGTM LN | 480 |
| CECKRGRFRI | KSGSLYMLCT | GNSSHSSWDN | QCQCTSSATR | NTTKQVTPQP | EEQKERKTTE | 540 |
| MQSPMQPV DQ | ASLPGHCREP | PWENEATER | IYHFVVGQMV | YYQCVQGYRA | LHRGPAESVC | 600 |
| KMTHGKTRWT | QPQLICTSGG | GGSGGGSGGG | GGSGGGSAPT | SSSTKKTQLQ | LEHLLLDLQM | 660 |
| ILNGINNYKN | PKLTRMLTFK | FYMPKKATEL | KHLQCLEEEL | KPLEEVLNLA | QSKNFHLRPR | 720 |
| DLISNINIV | LELKGSETTF | MCEYADETAT | IVEFLNRWIT | FCQSIISTLT | | 770 |

SEQ ID NO: 371 moltype = AA length = 530
FEATURE Location/Qualifiers
source 1..530
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 371

| | | | | | | |
|-------------|------------|------------|------------|------------|-------------|-----|
| DTVLTQSPAL | AVSPGERVTI | SCRASESVRT | GVHWYQQKPG | QQPKLLIYGA | SNLESGVPAR | 60 |
| FSGSGGTD F | TLTIDPVEAD | DTATYFCQQS | WNDPFTFGSG | TKLEIKRTVA | APSVFIFPPS | 120 |
| DEQLKSGTAS | VVCLLNNFYP | REAKVQWKVD | NALQSGNSQE | SVTEQDSKDS | TYSLSSTLTL | 180 |
| SKADYEKHKV | YACEVTHQGL | SSPVTKSFNR | GECELCDDDP | PEIPHATFKA | MAYKEGTM LN | 240 |
| CECKRGRFRI | KSGSLYMLCT | GNSSHSSWDN | QCQCTSSATR | NTTKQVTPQP | EEQKERKTTE | 300 |
| MQSPMQPV DQ | ASLPGHCREP | PWENEATER | IYHFVVGQMV | YYQCVQGYRA | LHRGPAESVC | 360 |
| KMTHGKTRWT | QPQLICTSGG | GGSGGGSGGG | GGSGGGSAPT | SSSTKKTQLQ | LEHLLLDLQM | 420 |
| ILNGINNYKN | PKLTRMLTFK | FYMPKKATEL | KHLQCLEEEL | KPLEEVLNLA | QSKNFHLRPR | 480 |
| DLISNINIV | LELKGSETTF | MCEYADETAT | IVEFLNRWIT | FCQSIISTLT | | 530 |

SEQ ID NO: 372 moltype = AA length = 536
FEATURE Location/Qualifiers
source 1..536
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 372

| | | | | | | |
|------------|------------|------------|------------|------------|------------|----|
| DTVLTQSPAL | AVSPGERVTI | SCRASESVRT | GVHWYQQKPG | QQPKLLIYGA | SNLESGVPAR | 60 |
|------------|------------|------------|------------|------------|------------|----|

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FSGSGSGTDF TLTIDPVEAD DTATYFCQQS WNDPPTFGSG TKLEIKRTVA APSVFIFPPS 120
DEQLKSGTAS VVCLLNNFYP REAKVQWKVD NALQSGNSQE SVTEQDSKDS TYSLSSTLTL 180
SKADYEKHKV YACEVTHQGL SSPVTKSFNR GECSGGGGSE LCDDDPPEIP HATFKAMAYK 240
EGTMLNCECK RGFRRIKSGS LYMLCTGNSS HSSWDNQCQC TSSATRNTTK QVTPQPEEQK 300
ERKTTMQSP MQPVDQASLP GHCREPPPWE NEATERIYHF VVGQMVYYQC VQGYRALHRG 360
PAESVCKMTH GKTRWTQPQL ICTSGGGGSG GGGSGGGGSG GGSAPTSST KKTQLQLEHL 420
LDDLQMLNG INNYKNPKLT RMLTFKPYMP KKATELKLQ CLEELKPLE EVLNLAQSKN 480
FHLRPRDLIS NINVIVLELK GSETTFMCEY ADETATIVEFL LNRWITFCQS IISTLT 536

```

```

SEQ ID NO: 373          moltype = AA length = 448
FEATURE                Location/Qualifiers
source                  1..448
                        mol_type = protein
                        organism = Synthetic construct

```

```

SEQUENCE: 373
EVQLLESGGG LVQPQGLRL SCAASGFTFK SYAMTWVRQA PGKGLEWVSA IVYSGGSTYY 60
ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAKYT RASYFYDAMD VWGQGTTVTV 120
SSASTKGPSV FPLAPCSRST SESTAALGCL VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ 180
SSGLYSLSSV VTPVSSSLGT KTYTCNVDPK PSNTKVDKRV ESKYGPCCP CPAPPELGGP 240
SVFLPPPCKP DTLMISRTP VTCVVVDVDSQ EDPEVQFNWY VDGVEVHNAK TKPREEQFNS 300
TYRVVSVLTV LHQDWLNGKE YKCKVSNKGL PSSIEKTISK AKGQPREPQV YTLPPSQEEM 360
TKNQVSLTCL VKGFYPSDIA VEWESNGQPE NNYKTTTPVL DSDGSFFLYS RLTVDKSRWQ 420
EGNVFSCSVM HEALHNYHTQ KSLSLSLG 448

```

```

SEQ ID NO: 374          moltype = AA length = 213
FEATURE                Location/Qualifiers
source                  1..213
                        mol_type = protein
                        organism = Synthetic construct

```

```

SEQUENCE: 374
DTVLTQSPAL AVSPGERVTI SCRASESVRT GVHWYQQKPG QPKLLIYGA SNLESGVPAR 60
FSGSGSGTDF TLTIDPVEAD DTATYFCQQS WNDPPTFGSG TKLEIKRTVA APSVFIFPPS 120
DEQLKSGTAS VVCLLNNFYP REAKVQWKVD NALQSGNSQE SVTEQDSKDS TYSLSSTLTL 180
SKADYEKHKV YACEVTHQGL SSPVTKSFNR GEC 213

```

```

SEQ ID NO: 375          moltype = AA length = 585
FEATURE                Location/Qualifiers
source                  1..585
                        mol_type = protein
                        organism = Synthetic construct

```

```

SEQUENCE: 375
EVQLQQSGPE LVKPGASVKI SCKTSGYTFT EYTMHWVKQS HGKSLEWIGG INPNNGTTY 60
NQKFRGKATL TVDKSSSTAY MELRSLTSQD SAVYYCARDY YRYGHYYAMD YWGQTSVTV 120
SSAKTTPPSV YPLAPGSAQ TNSMVTLGCL VKGYFPEPVT VTWNSGSLSS GVHTFPAVLQ 180
SDLYTLSSSV TVPSSTWPE TVTCNVAHPA SSTKVDKIV PRDCGCKPCI CTVPEVSSVF 240
IFPPKPKDVL TITLTPKVT VVVAISKDDP EVQFSWFVDD VEVHTAQTQP RBEQFNSTR 300
SVSELPIMHQ DWLNGKEFKC RVNSAAFPAP IEKTISKTKG RPKAPQVYTI PPPKEQMAKD 360
KVSFLTCMID FFPEDITVEW QWNGQPAENY KNTQPIMDTD GSYFVYSKLN VQKSNWEAGN 420
TFTCSVLHEG LHNHTEKSL SHSPGKSGGG GSAPTSSSTK KTQLQLEHL LDLQMLNGI 480
NNYKNPKLTR MLTFKPYMPK KATELKLQ CLEELKPLE VLNLAQSKNF HLRPRDLISN 540
INVIVLELKG SETTFMCEYA DETATIVEFL NRWITFCQSI IISTLT 585

```

```

SEQ ID NO: 376          moltype = AA length = 213
FEATURE                Location/Qualifiers
source                  1..213
                        mol_type = protein
                        organism = Synthetic construct

```

```

SEQUENCE: 376
QIVLTQSPAI MSASPGEKVT MTCVSSSVR FMHWYQQKSG TSPKRWIYDT SKLASGVPAR 60
FSGSGSGTSS SLTISSMEAE DAATYYCQQW SNNPPTFGG TKLKIKRADA APTVSIFFPS 120
SEQLTSGGAS VVCFLLNFYP KDINVKWKID GSERQNGVLN SWTDQDSKDS TYSMSSTLTL 180
TKDEYERHNS YTCEATHKTS TSPIVKSFNR NEC 213

```

```

SEQ ID NO: 377          moltype = AA length = 133
FEATURE                Location/Qualifiers
source                  1..133
                        mol_type = protein
                        organism = Synthetic construct

```

```

SEQUENCE: 377
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCLSIIS TLT 133

```

```

SEQ ID NO: 378          moltype = AA length = 133
FEATURE                Location/Qualifiers
source                  1..133
                        mol_type = protein
                        organism = Synthetic construct

```

```

SEQUENCE: 378

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-continued

SEQUENCE: 384
EVQLLESGGG LVQPGGSLRL SCAASGFTFK DYCMTWVRQA PGKGLEWVSA IVYSGGSTYY 60
ADSVKGRFTI SRDNSKNTLY LQMNLRRAED TAVYYCAKYT RASYFYDAMD VWGQGTTVTV 120
SS 122

SEQ ID NO: 385 moltype = AA length = 109
FEATURE Location/Qualifiers
source 1..109
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 385
EIVLTQSPGT LSLSPGERAT LSCRASQSIG KSFLLAWYQOK PGQAPRLLIY DASTRAADIP 60
ARFSGSGSGT DFTLTISLE PEDFAVYVCQ QYYDWPPLSF GGGTKVEIK 109

SEQ ID NO: 386 moltype = AA length = 10
FEATURE Location/Qualifiers
source 1..10
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 386
GFTFKDYCMT 10

SEQ ID NO: 387 moltype = AA length = 17
FEATURE Location/Qualifiers
source 1..17
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 387
AIVYSGGSTY YADSVKG 17

SEQ ID NO: 388 moltype = AA length = 13
FEATURE Location/Qualifiers
source 1..13
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 388
YTRASIFYDA MDV 13

SEQ ID NO: 389 moltype = AA length = 12
FEATURE Location/Qualifiers
source 1..12
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 389
RASQSIGKSF LA 12

SEQ ID NO: 390 moltype = AA length = 7
FEATURE Location/Qualifiers
source 1..7
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 390
DASTRAA 7

SEQ ID NO: 391 moltype = AA length = 10
FEATURE Location/Qualifiers
source 1..10
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 391
QQYYDWPPLS 10

SEQ ID NO: 392 moltype = DNA length = 363
FEATURE Location/Qualifiers
source 1..363
 mol_type = other DNA
 organism = Synthetic construct

SEQUENCE: 392
caggttcagc tggttcagtc tggcagcgag ctgaagaaac ctggcgccct tgtgaagggtg 60
tctctgcaagg cctctggcta cagcctgtac ggcacctcta tgcactgggt cggacaggct 120
ccaggacagg gacttgagtg gatgggctac atcagcccct ttaccggcag agccacatac 180
gcccaggggt tcacaggcag attcgtgttc agcctggaca ccagcgtgtc cacagcctac 240
ctgcagatca gctctctgaa ggccgaggac accgcccgtg actactgcgc cagagactac 300
gactaccggt actactatgc catggactac tggggccagg gcaccacagt tacagtgtcc 360
tca 363

SEQ ID NO: 393 moltype = DNA length = 324
FEATURE Location/Qualifiers
source 1..324

-continued

```

mol_type = other DNA
organism = Synthetic construct

SEQUENCE: 393
gaaattgtgc tgacacagag ccccgacttc cagagcgtga cccctaaaga aaaagtgacc 60
atcacctgta ccgccagcga gtccgtgcct cctcagttcc tgcattggta tcagcagaag 120
cccgatcaga gcccacaagct gctgatctac gccagcagag aaagagccag cggcgtccca 180
agcagathtt ctggctctgg cagcggcacc gacttcacc tgacaatcaa tagcctgtaa 240
gccgaggacg ccgccaccta ctactgccac cagtttcaca gaagccctct gacctttggc 300
ggaggcacca agctggaat caag 324

SEQ ID NO: 394      moltype = AA length = 121
FEATURE           Location/Qualifiers
source           1..121
                 mol_type = protein
                 organism = Synthetic construct

SEQUENCE: 394
QVQLVQSGSE LKKPGASVKV SCKASGYSLY GTSMHWRQA PGQGLEWMGY ISPFTGRATY 60
AQQFTGRFV SLDTSVSTAY LQISLKAED TAVYYCARDY DYRYYYAMDY WQGTTTVTS 120
S 121

SEQ ID NO: 395      moltype = AA length = 108
FEATURE           Location/Qualifiers
source           1..108
                 mol_type = protein
                 organism = Synthetic construct

SEQUENCE: 395
EIVLTQSPDF QSVTPKEKVT ITCASESVP PQFLHWYQQK PDQSPKLLIY ASRERASGVP 60
SRFSGSGSGT DFTLTINSLE AEDAATYYCH QFHRSPLTFG GGTKLEIK 108

SEQ ID NO: 396      moltype = AA length = 10
FEATURE           Location/Qualifiers
source           1..10
                 mol_type = protein
                 organism = Synthetic construct

SEQUENCE: 396
GYSLYGTSMH 10

SEQ ID NO: 397      moltype = AA length = 17
FEATURE           Location/Qualifiers
source           1..17
                 mol_type = protein
                 organism = Synthetic construct

SEQUENCE: 397
YISPFTGRAT YAQGFTG 17

SEQ ID NO: 398      moltype = AA length = 12
FEATURE           Location/Qualifiers
source           1..12
                 mol_type = protein
                 organism = Synthetic construct

SEQUENCE: 398
DYDYRYYYAM DY 12

SEQ ID NO: 399      moltype = AA length = 12
FEATURE           Location/Qualifiers
source           1..12
                 mol_type = protein
                 organism = Synthetic construct

SEQUENCE: 399
TASESVPPQF LH 12

SEQ ID NO: 400      moltype = AA length = 7
FEATURE           Location/Qualifiers
source           1..7
                 mol_type = protein
                 organism = Synthetic construct

SEQUENCE: 400
ASRERAS 7

SEQ ID NO: 401      moltype = AA length = 9
FEATURE           Location/Qualifiers
source           1..9
                 mol_type = protein
                 organism = Synthetic construct

SEQUENCE: 401
HQFHRSPLT 9

SEQ ID NO: 402      moltype = DNA length = 345
FEATURE           Location/Qualifiers

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source                1..345
                      mol_type = other DNA
                      organism = Synthetic construct

SEQUENCE: 402
gacgtgcagc  tgggtgaaag  cggcggaggc  ctggtocagc  cggcgggctc  tctgagactg  60
agctgcgccg  ccagcggctt  caccttcgac  atcagcgcca  tgagctgggt  gcggcaggcc  120
cctggcaagg  gcctggaatg  ggtcagcaca  atcagcggat  ctgcctacag  cacctactac  180
gccgacagcg  tgaagggcag  attcaccatc  tcaagagata  acagcaagag  caccctgtac  240
ctgcagatga  acagcctgcg  ggcggaggac  accgccgtgt  actactgcgc  cagagagatc  300
ttcagcgact  actggggctt  gggcaccctg  gtgacagtgt  cctca                345

SEQ ID NO: 403        moltype = DNA  length = 330
FEATURE              Location/Qualifiers
source                1..330
                      mol_type = other DNA
                      organism = Synthetic construct

SEQUENCE: 403
caaagcgtgc  tgacacagcc  ccccagcgc  tctggcacc  ctggccagag  agtgaccatc  60
tcatgcagcg  ggtcaacaag  caacatcggc  agagagagcg  tgtactggta  ccagcagctg  120
cctggaaccg  cccctaagct  gctgatctac  agcaacgtgc  agcggcctag  cggcgcccct  180
aacagattca  gcggcagcaa  gagcggcacc  agcggcagcc  tggccatcag  cggcctgcag  240
agcgaggacg  aggccgacta  ctactgcgcg  acatgggacg  acagcctgaa  cggctgggtg  300
ttcggcggcg  gaactaagct  gaccgtccta                330

SEQ ID NO: 404        moltype = AA  length = 115
FEATURE              Location/Qualifiers
source                1..115
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 404
DVQLVESGGG  LVQPGGSLRL  SCAASGFTFD  ISAMSWVRQA  PGKGLEWVST  ISGSAYSTYY  60
ADSVKGRFTI  SRDNSKSTLY  LQMNLSLRAE  TAVYYCAREI  FSDYWGLGTL  VTVSS        115

SEQ ID NO: 405        moltype = AA  length = 110
FEATURE              Location/Qualifiers
source                1..110
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 405
QSVLTQPPSA  LVQPGQRVTI  SCSGSTSNI  RESVYVYQQL  PGTAPKLLIY  SNVQRPSGAP  60
NRFSGSKSGT  SASLAISGLQ  SEDEADYYCG  TWDDSLNGWV  FGGGTKLTVL                110

SEQ ID NO: 406        moltype = AA  length = 10
FEATURE              Location/Qualifiers
source                1..10
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 406
GFTFDISAMS                10

SEQ ID NO: 407        moltype = AA  length = 17
FEATURE              Location/Qualifiers
source                1..17
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 407
TISGSAYSTY  YADSVKG                17

SEQ ID NO: 408        moltype = AA  length = 6
FEATURE              Location/Qualifiers
source                1..6
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 408
EIFSDY                6

SEQ ID NO: 409        moltype = AA  length = 13
FEATURE              Location/Qualifiers
source                1..13
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 409
SGSTSNIGRE  SVY                13

SEQ ID NO: 410        moltype = AA  length = 7
FEATURE              Location/Qualifiers
source                1..7
                      mol_type = protein
                      organism = Synthetic construct

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SEQUENCE: 410
SNVQRPS 7

SEQ ID NO: 411 moltype = AA length = 11
FEATURE Location/Qualifiers
source 1..11
mol_type = protein
organism = Synthetic construct

SEQUENCE: 411
GTWDDSLNGW V 11

SEQ ID NO: 412 moltype = DNA length = 1755
FEATURE Location/Qualifiers
source 1..1755
mol_type = other DNA
organism = Synthetic construct

SEQUENCE: 412
gaggtgcagc tgctggaagg cggcggcggc ctctgcagc ctggcggatc tctgcccgtg 60
agctgtgctg ccagcggcgt cacatttaa tctacgcca tgcactgggt tagacaagcc 120
cccggaaaagg gcctggaatg ggtgtccgcc atcgtctaca gcggcggatc tacatactac 180
gcccacagcg tgaagggcgg gttcaccatc agcagagata atagcaagaa caccctgtac 240
ctgcagatga acagcctgag agccaggagc accgcccgtg actactgcgc caagtaacgac 300
agagcttctt atttctacga tgccatggac gtgtggggcc agggcaccac cgtgacagtg 360
tctctcagta gcaccaaggg ccctagcgtg ttccactgg cccctagctc taaaagcaca 420
agcggcggaa ccgcccgtct gggttgtctg gtgaaaggact acttccctga gcctgtgacc 480
gtcagctgga acagcggcgc cctgaccagc ggcgttcaca cattccccgc tgtgctgcag 540
agctctgggc tgtacagcct gaggcagcgt gtgaccgtgc cttctcttc tctgggcaca 600
caaacataca tctgcaacgt gaaccacaag ccagtaata ccaagtgga taagaaggtg 660
gaacctaaat cttgccaaga gacccacacc tgctctcctg gccctgctcc tgaactggct 720
ggagctccca gcctgttctc gttccccccc aaacctaaag acaccctgat gatcagccgg 780
accctgagg tgacctcgtg ggtcgtcgac gtgtccacg aagatcctga ggtgaagttc 840
aactggtacg tggcggcgtg ggaagtgcac aatgccaaaga caaagcctag agaggaacag 900
tacaacagca cctatagagt ggtgtccgtg ctgacagtgc tgcaccagga ctggctgaac 960
ggcaaggaat acaagtgcga ggtgtccaac aaggccctcc cgcctctat cgagaagacc 1020
atcagcaagg caaagggcca acctagagag ccccaggtgt acaccctgcc tccaagcaga 1080
gatgagctga ccaagaacca ggttagcctg actgtctctg tgaaggcctt ctaccctcc 1140
gatctcgcgc tccaatggga gaggcaacgc cagcctgaga acaactacaa gaccacacct 1200
ccagtgtgg acagcagcgg cagcttcttc ctgtatagca agctgacagt ggacaagagc 1260
agatggcagc agtgcaacgt gttcagctgc agcgtcatgc acgagccct gcacaaccac 1320
tacaccaga agtctctgag cctgagccct ggaaaggccc ctgcttctag cagcaccacg 1380
aagaccacgc tgcagctgga acacctgctg ctggccctgc agatgatcct gaacggcatc 1440
aacaactaca agaaccocaa gctgaccgag atgctgacat ttaagttcta catgcctaag 1500
aaagccaccg agctgaaagt cctgcaatgt ctggaagaag agctgaaacc tctggaagag 1560
gtgctgaatc tggctcagtc aaagaacttc caccttagac ctagagatct gatcagcaac 1620
atcaactgta tctgtctgga actgaagggc agcagagcga ccttcatgtg cgagtacgcc 1680
gacgagacag ccacaactgt ggagttcctg aacagatgga tcacctcgc ccagagcattc 1740
atctccacc tgacc 1755

SEQ ID NO: 413 moltype = DNA length = 648
FEATURE Location/Qualifiers
source 1..648
mol_type = other DNA
organism = Synthetic construct

SEQUENCE: 413
gagatcgtgc tgaccacgctc cccaggcaca ctgagcctga gcccccggcga gcggggccacc 60
ctgagctgta gagctagcca gagcatctcc agcagcttcc tggcctggta ccagcagaaa 120
cctggccagg cccctagact gctgatctac gacgcctctg atagagctac aggcattcccc 180
gaccggttca gcggcagcgg atctggcacc gacttcaccc tgaccatcag cagactcgag 240
cctgaagatt tgcgccgtgta ctactgccag caatactatg actggcctcc tctgtctttt 300
ggcggcggaa caaaggtgga aataaagcgt acgggtggcgg cgcccagcgt gttcatcttc 360
ccaccacgag acgagcagct gaagtccggc acagccagcg tgggtgacct gctgaacaac 420
ttctaccccc gcgaggccaa ggtgcagtgg aaggtggaca acgcccctgca gagcggcaac 480
agccaggaaa gcgtgaccga gcaggacagc aaggactcca cctacagcct gagcagcacc 540
ctgaccctga gcaaggccga ctacgagaag cacaaggtgt acgcttcgca agtgaccacc 600
cagggcctgt ccagccccgt gaccaagagc ttcaaccggg gcgagtgcc 648

SEQ ID NO: 414 moltype = AA length = 451
FEATURE Location/Qualifiers
source 1..451
mol_type = protein
organism = Synthetic construct

SEQUENCE: 414
EVQLLESGGG LVQPGGSLRL SCAASGFTFK SYAMHWVRQA PGKLEWVSA IVYSGGSTYY 60
ADSVKGRFTI SRDMSKNTLY LQMNSLRAED TAVYYCAKYD RASYFYDAMD VWGQGTFTTV 120
SSASTKGPSV FPLAPSSKST SGGTAALGCL VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ 180
SSGLYSLSSV VTPSSSLGT QTYICNVNHNK PSNTKVDKVK EPKSCDKTHT CPPCPAPELA 240
GAPSVFLFPP KPKDTLMISR TPEVTCVVVD VSHEDPEVKF NWFYVDGVEVH NAKTKPREEQ 300
YNSTYRVVSV LTVLHQDWLNL KEYKCKVSN KALPAPIEKT ISKAKGQPRE PQVYTLPPSR 360
DELTKNQVSL TCVLKGFYPS DIAVEWESNG QPENNYKTTT PVLDSGQSFY LYSKLTVDKS 420

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| | | | | |
|----------------|--------------------------------|------------|----------------|---------------|
| RWQQGNVFS | SVMHEALHNNH | YTQKSLSLSP | G | 451 |
| SEQ ID NO: 415 | moltype = AA length = 216 | | | |
| FEATURE | Location/Qualifiers | | | |
| source | 1..216 | | | |
| | mol_type = protein | | | |
| | organism = Synthetic construct | | | |
| SEQUENCE: 415 | | | | |
| EIVLTQSPGT | LSLSPGERAT | LSCRASQ | SIS SSFLAWYQ | QK PGQAPRLLIY |
| DRFSGSGSGT | DFTLTISRLE | PEDFAVY | CQ QYDWPPLSF | GGGTKVEIKR |
| PPSDEQLKSG | TASVVCLLNN | FYPREAK | VQW KVDNALQSGN | SQESVTEQDS |
| LTLKADYK | HKVYACEVTH | QGLSSPV | TKS FNRGEC | 216 |
| SEQ ID NO: 416 | moltype = AA length = 122 | | | |
| FEATURE | Location/Qualifiers | | | |
| source | 1..122 | | | |
| | mol_type = protein | | | |
| | organism = Synthetic construct | | | |
| SEQUENCE: 416 | | | | |
| EVQLLESGGG | LVQPGGSLRL | SCAASGFT | PK SYAMHWVRQA | PGKGLEWVSA |
| ADSVKGRFTI | SRDNSKNTLY | LQMNSLRA | ED TAVYYCAKYD | RASYFYDAMD |
| SS | | | | VWGQGT |
| | | | | TVTV 122 |
| SEQ ID NO: 417 | moltype = AA length = 109 | | | |
| FEATURE | Location/Qualifiers | | | |
| source | 1..109 | | | |
| | mol_type = protein | | | |
| | organism = Synthetic construct | | | |
| SEQUENCE: 417 | | | | |
| EIVLTQSPGT | LSLSPGERAT | LSCRASQ | SIS SSFLAWYQ | QK PGQAPRLLIY |
| DRFSGSGSGT | DFTLTISRLE | PEDFAVY | CQ QYDWPPLSF | GGGTKVEIK |
| | | | | 60 |
| | | | | 109 |
| SEQ ID NO: 418 | moltype = AA length = 10 | | | |
| FEATURE | Location/Qualifiers | | | |
| source | 1..10 | | | |
| | mol_type = protein | | | |
| | organism = Synthetic construct | | | |
| SEQUENCE: 418 | | | | |
| GFTFKSYAMH | | | | 10 |
| SEQ ID NO: 419 | moltype = AA length = 17 | | | |
| FEATURE | Location/Qualifiers | | | |
| source | 1..17 | | | |
| | mol_type = protein | | | |
| | organism = Synthetic construct | | | |
| SEQUENCE: 419 | | | | |
| AIVYSGGSTY | YADSVKG | | | 17 |
| SEQ ID NO: 420 | moltype = AA length = 13 | | | |
| FEATURE | Location/Qualifiers | | | |
| source | 1..13 | | | |
| | mol_type = protein | | | |
| | organism = Synthetic construct | | | |
| SEQUENCE: 420 | | | | |
| YDRASYFYDA | MDV | | | 13 |
| SEQ ID NO: 421 | moltype = AA length = 12 | | | |
| FEATURE | Location/Qualifiers | | | |
| source | 1..12 | | | |
| | mol_type = protein | | | |
| | organism = Synthetic construct | | | |
| SEQUENCE: 421 | | | | |
| RASQSISSSF | LA | | | 12 |
| SEQ ID NO: 422 | moltype = AA length = 7 | | | |
| FEATURE | Location/Qualifiers | | | |
| source | 1..7 | | | |
| | mol_type = protein | | | |
| | organism = Synthetic construct | | | |
| SEQUENCE: 422 | | | | |
| DASDRAT | | | | 7 |
| SEQ ID NO: 423 | moltype = AA length = 10 | | | |
| FEATURE | Location/Qualifiers | | | |
| source | 1..10 | | | |
| | mol_type = protein | | | |
| | organism = Synthetic construct | | | |
| SEQUENCE: 423 | | | | |
| QQYYDWPPLS | | | | 10 |

-continued

SEQ ID NO: 424 moltype = AA length = 448
FEATURE Location/Qualifiers
source 1..448
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 424
EVQLLESQGGG LVQPGGSLRL SCAASGFTFK DYCMTWVRQA PGKGLEWVSA IVYSGGSTYY 60
ADSVKGRFTI SRDNSKNTLY LQMNLRRAED TAVYYCAKYT RASYFYDAMD VWGQGTTVTV 120
SSASTKGPSV FPLAPCSRST SESTAALGCL VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ 180
SSGLYSLSSV VTPVSSSLGT KTYTCNVDPK PSNTKVDKRV ESKYGPCCPP CPAPEFLGGP 240
SVFLFPPKPK DTLMISRTPV VTCVVVDVDSQ EDPEVQFNWY VDGVEVHNAK TKPREEQFNS 300
TYRVVSVLTV LHQDWLNGKE YKCKVSNKGL PSSIEKTISK AKGQPREPQV YTLPPSQEEM 360
TKNQVSLTCL VKGFYPSDIA VEWESNGQPE NNYKTPPPVL DSDGSFFLYS RLTVDKSRWQ 420
EGNVFSCSVM HEALHNHYTQ KSLSLSLG 448

SEQ ID NO: 425 moltype = AA length = 216
FEATURE Location/Qualifiers
source 1..216
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 425
EIVLTQSPGT LSLSPGERAT LSCRASQSIG KSFLAWYQQK PGQAPRLLIY DASTRAADIP 60
ARFSGSGSGT DFTLTISLSE PEDFAVYCYQ QYYDWPPLSF GGGTKVEIKR TVAAPSVFIF 120
PPSDEQLKSG TASVVCLLNN FYPREAKVQW KVDNALQSGN SQESVTEQDS KDSTYLSLST 180
LTLKADYEEK HKVYACEVTH QGLSSPVTKS FNRGEC 216

SEQ ID NO: 426 moltype = AA length = 447
FEATURE Location/Qualifiers
source 1..447
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 426
QVQLVQSGSE LKKPGASVKV SCKASGYSLY GTSMHWRQA PGQGLEWNGY ISPFTGRATY 60
AQQFTGRFVF SLDTSVSTAY LQISSLKAED TAVYYCARDY DYRYYYAMDY WGQGTTVTVS 120
SASTKGPSVF FPLAPCSRST ESTAALGCLV KDYFPEPVTV SWNSGALTSV VHTFPAVLQS 180
SGLYSLSSVV TPVSSSLGTE TYTCNVDPK PSNTKVDKRV ESKYGPCCPP CPAPEFLGGP 240
VFLFPPKPKD TLMISRTPV VTCVVVDVDSQ EDPEVQFNWY VDGVEVHNAK KPREEQFNST 300
YRVVSVLTVL HQDWLNGKEY KCKVSNKGLP SSIKTIKSKA KGQPREPQV YTLPPSQEEM 360
KNQVSLTCLV KGFYPSDIAV EWSNGQPEN NYKTPPPVLD SDGSFFLYSR LTVDKSRWQE 420
GNVFCSCVMH EALHNHYTQK SLSLSLG 447

SEQ ID NO: 427 moltype = AA length = 215
FEATURE Location/Qualifiers
source 1..215
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 427
EIVLTQSPDF QSVTPKEKVT ITCTASESVP PQFLHWYQQK PDQSPKLLIY ASRERASGVP 60
SRFSGSGSGT DFTLTINSLE AEDAATYYCH QFHRSPLTFG GGTKLEIKRT VAAPSVFIFP 120
PSDEQLKSGT ASVVCLLNLF YPREAKVQWK VDNALQSGNS QESVTEQDSK DSTYLSLSTL 180
TLKADYEEKH KVYACEVTHQ GLSSPVTKSF NRGEC 215

SEQ ID NO: 428 moltype = AA length = 441
FEATURE Location/Qualifiers
source 1..441
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 428
DVQLVESGGG LVQPGGSLRL SCAASGFTFD ISAMSWVRQA PGKGLEWVST ISGSAYSTYY 60
ADSVKGRFTI SRDNSKNTLY LQMNLRRAED TAVYYCAREI FSDYWGGLTL VTVSSASTKG 120
PSVFPLAPCS RSTSESTAAL GCLVKDYFPE PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL 180
SSVTVPSST LGTKTYTCNV DHKPSNTKVD KRVESKYGPP CPPCPAPEFL GGPSVFLFPP 240
KPKDTLMISSR TPEVTCVVVD VSQEDPEVQF NNYVDGVEVH NAKTKPREEQ FNSTYRVVSV 300
LTVLHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQPRE PQVYTLPPSQ EEMTKNQVSL 360
TCLVKGFYPS DIAVEWESNG QPENNYKTP PVLDSGDSFF LYSRLTVDKS RWQEGNVFSC 420
SVMHEALHNH YTQKSLSLSL G 441

SEQ ID NO: 429 moltype = AA length = 216
FEATURE Location/Qualifiers
source 1..216
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 429
QSVLTQPPSA SGTGQQRVTI SCSGSTSNIG RESVYVYQQK PGTAPKLLIY SNVQRPSGAP 60
NRFSGSKSGT SASLAISGLQ SEDEADYCYG TWDDSLNGWV FGGGKTLTVL GQPKAAPSVT 120
LFPSSSEELQ ANKATLVCLI SDFYPGAVTV AWKADSSPVK AGVETTTPSK QSNNKYAASS 180
YLSLTPEQWK SHRSYSQVPT HEGSTVEKTV APTKCS 216

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SEQ ID NO: 430 moltype = AA length = 582
 FEATURE Location/Qualifiers
 source 1..582
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 430
 EVQLLESGGG LVQPGGSLRL SCAASGFTFK DYCMTWVRQA PGKGLEWVSA IVYSGGSTYY 60
 ADSVKGRFTI SRDNSKNTLY LQMNLRRAED TAVYYCAKYT RASYFYDAMD VWGQGTTVTV 120
 SSASTKGPSV FPLAPCSRST SESTAALGCL VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ 180
 SSGLYSLSSV VTPSSSLGT KTYTCNVDPK PSNTKVDKRV ESKYGPCCPP CPAPEFLGGP 240
 SVFLFPPKPK DTLMISRTPV VTCVVVDVDSQ EDPEVQFNWY VDGVEVHNAK TKPREEQFNS 300
 TYRVVSVLTV LHQDNLNGKE YKCKVSNKGL PSSIEKTISK AKGQPREPQV YTLPPSQEEM 360
 TKNQVSLTCL VKGFYPSDIA VEWESNGQPE NNYKTPPVLD DSDGSFFLYS RLTVDKSRWQ 420
 EGNVFCSSVM HEALHNHYTQ KSLSLSLGKA PTSSTKKTQ LQLEHLLAL QMILNGINNY 480
 KNPKLEMLT FKFYMPKAT ELKHLQCLEE ELKPLEEVLN LAQSKNPHLR PRDLISINIV 540
 IVLELKGSET TFMCEYADET ATIVEFLNRW ITFCQSIIST LT 582

SEQ ID NO: 431 moltype = AA length = 585
 FEATURE Location/Qualifiers
 source 1..585
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 431
 EVQLLESGGG LVQPGGSLRL SCAASGFTFK SYAMHWVRQA PGKGLEWVSA IVYSGGSTYY 60
 ADSVKGRFTI SRDNSKNTLY LQMNLRRAED TAVYYCAKYD RASYFYDAMD VWGQGTTVTV 120
 SSASTKGPSV FPLAPSSKST SGGTAALGCL VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ 180
 SSGLYSLSSV VTPSSSLGT QTYICNVNHHK PSNTKVDKRV EPKSCDKTHT CPPCPAPELA 240
 GAPSVFLFPP KPKDTLMISR TPEVTCVVVD VSHEDPEVKF NNYVDGVEVH NAKTKPREEQ 300
 YNSTYRVVSV LTVLHQDNLN GKEYKCKVSN KALPAPIEKT ISKAKGQPRE PQVYTLPPSR 360
 DELTKNQVSL TCVKGFYPS DIAVEWESNG QPENNYKTP PVLDSDGSFF LYSKLTVDKS 420
 RWQKGNVFCSSVMHEALHNHYTQKSLSLSLGKA GKAPASSSTK KTQLQLEHLL LQLQMLNGI 480
 NNYKNPKLTR MLTFKPYMPK KATELKHLC LEEELKPLEE VLNLAQSKNF HLRPRDLISN 540
 INVIVLELKG SETTFMCEYA DETATIVEFL NRWITFAQSI ISTLT 585

SEQ ID NO: 432 moltype = AA length = 587
 FEATURE Location/Qualifiers
 source 1..587
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 432
 QVQLVQSGSE LKPKGASVKV SCKASGYSLY GTSMHWRQA PGQGLEWVMGY ISPFTGRATY 60
 AQQFTGRFVF SLDTSVSTAY LQISSLKAED TAVYYCARYD DRYYYAMDY WGQGTTVTVS 120
 SASTKGPSVF PLAPCSRSTS ESTAALGCLV KDYFPEPVTV SWNSGALTSV VHTFPAVLQS 180
 SGLYSLSSVV VTPSSSLGK TYTCNVDPK PSNTKVDKRV ESKYGPCCPP PAPEFLGGPS 240
 VFLFPPKPKD TLMISRTPV TCVVVDVDSQ DPEVQFNWY DGVVHNAKT KPREEQFNST 300
 YRVVSVLTVL HQDNLNGKEY CKKVSNGKLP SIEKTISKA KGQPREPQVY TLPPSQEEMT 360
 KNQVSLTCLV KGFYPSDIAV EWESNGQPEN NYKTPPVLD SDGSFFLYSR RLTVDKSRWQ 420
 GNVFCSSVMH EALHNHYTQK SLSLSLGKSG GGSAPTSSS TKKTQLQLEH LLLALQMLN 480
 GINNYKNPKL TMLTFKPYM PKKATELKHLC LEEELKPLEE EEVNLAQSK NPHLRPRDLI 540
 SNINIVLEL KGSETTFMCE YADETATIVE FLNRWITFCQ SIISTLT 587

SEQ ID NO: 433 moltype = AA length = 575
 FEATURE Location/Qualifiers
 source 1..575
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 433
 DVQLVESGGG LVQPGGSLRL SCAASGFTFD ISAMSWVRQA PGKGLEWVST ISGSAYSTYY 60
 ADSVKGRFTI SRDNSKSTLY LQMNLRRAED TAVYYCAREI PSDYWGLGTL VTVSSASTKG 120
 PSVFLAPCS RSTSESTAAL GCLVKDYFPE PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL 180
 SSVVTPSSSS LGTKYTCNV DHPKPSNTKVD KRVESKYGPP CPPCPAPEFL GGPSVFLFPP 240
 KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NNYVDGVEVH NAKTKPREEQ FNSTYRVVSV 300
 LTVLHQDNLN GKEYKCKVSN KGLPSSIEKT ISKAKGQPRE PQVYTLPPSQ EEMTKNQVSL 360
 TCVKGFYPS DIAVEWESNG QPENNYKTP PVLDSDGSFF LYSRLTVDKS RWQEGNVFSC 420
 SVMHEALHNHYTQKSLSLSLGKA KAPTSSSTK KTQLQLEHLL LALQMLNGI NNYKNPKLTE 480
 MLTFKPYMPK KATELKHLC LEEELKPLEE VLNLAQSKNF HLRPRDLISN INVIVLELKG 540
 SETTFMCEYA DETATIVEFL NRWITFCQSI ISTLT 575

SEQ ID NO: 434 moltype = AA length = 577
 FEATURE Location/Qualifiers
 source 1..577
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 434
 EVQLVESGGG LVQPGRSLLK SCAVSGFTFS DYAMAWVRQA PKKGLEWVAT ISYDGSRTYY 60
 RDSVKGRFTI SRDNAKITLY LQMDLSRSED TATYYCARHG SGYFDYWGQG VMVTVSSAST 120
 KGPSVFLAP CSRSTSESTA ALGCLVKDYF PEPVTVSWNS GALTSGVHTF PAVLQSSGLY 180
 SLSSVTVVPS SSLGKTYTC NVDPKPSNTK VDKRVESKYG PPCPPAPE FLGGPSVFLF 240
 PPKPKDTLMI SRTPEVTCVV VDVSDPEDEV QFNWYVDGVE VHNKTKPRE EQPNSTYRVV 300

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SEQUENCE: 440
EVQLLESQGGG LVQPGGSLRL SCTASGFTFS SYEMQWVRQA PGKGLEWVLG ITSSSSHFY 60
ADSVKGRFTV SRDNSKNTLY LQMNSLRAED TAVYYCTKDL NSYGLDVGW QGTTVTVSSA 120
STKGPSVFPPL APCSRSTSES TAALGCLVKD YFPEPVTVSW NSGALTSQVH TTPAVLQSSG 180
LYSLSSVVTV PSSSLGTKTY TCNVDHKPSN TKVDKRVESK YGPPCPPCPA PEPFLGGPSVF 240
LFPPPKPDTL MISRTPEVTC VVVDVSDQEDP EVQFNWYVDG VEVHNAKTKP RREEQFNSTYR 300
VVSVLTVLHQ DWLNGKLEYK KVSNGKLPSS IEKTIKAKG QPREPQVYTL PPSQEMTKN 360
QVSLTCLVKG FYPSPDIAVEW ESNQGPENNY KTTTPVLDSG GSFFLYSRLT VDKSRWQEGN 420
VFSCSVMHEA LHNHYTQKSL SLSLG 445

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SEQ ID NO: 441      moltype = AA length = 216
FEATURE           Location/Qualifiers
source           1..216
                 mol_type = protein
                 organism = Synthetic construct

```

```

SEQUENCE: 441
QSVMTQPPSA SGTGQQRVTI SCSSGTSNLG NNYVSWYQHL PGTAPKLLIY GNDQRPSGVP 60
DRFSGSKSGT SASLAISGLQ SDDEADYICS SWDASLNVWV FGGGKTLTVL GQPKAAPSVT 120
LFPPSSSEELQ ANKATLVCLI SDFYPGAVTV AWKADSSPVK AGVETTTPSK QSNNKYAASS 180
YLSLTPEQWK SHRSYSCQVT HEGSTVEKTV APTECS 216

```

```

SEQ ID NO: 442      moltype = AA length = 448
FEATURE           Location/Qualifiers
source           1..448
                 mol_type = protein
                 organism = Synthetic construct

```

```

SEQUENCE: 442
EVQLLESQGGG LVQPGGSLRL SCAASGFTFS DYYMSWVRQA PGKGLEWVSA ISSSGGTIFY 60
ADSVKGRFII SRDNSKNTLY LQMNSLRAED TAVYYCAKHK WNDVYDAMD VWGQGTTVTV 120
SSASTKGPSV VPLAPCSRST SESTAALGCL VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ 180
SSGLYSLSSV VTPSSSLGT KTYTCNVDHK PSNTKVDKRV ESKYGPCCPP CPAPEPLGGP 240
SVFLPPPDKP DTLMISRTPE VTCVVVDVSDQ EDPEVQFNWY VDGVEVHNAK TKPREEQFNS 300
TYRVVSVLTV LHQDWLNGKE YKCKVSNKGL PSSIEKTISK AKGQPREPQV YTLPPSQEEM 360
TKNQVSLTCL VKGFYPSDIA VEWESNGQPE NNYKTTTPVL DSDGSFFLYS RLTVDKSRWQ 420
EGNVFSCSVM HEALHNHYTQ KLSLSLSLG 448

```

```

SEQ ID NO: 443      moltype = AA length = 216
FEATURE           Location/Qualifiers
source           1..216
                 mol_type = protein
                 organism = Synthetic construct

```

```

SEQUENCE: 443
QSVLTQPPSA SGTGQQRVTI SCSSGNSNIG RNLVNWYQQL PGTAPKLLIY TVDQRPSGVP 60
DRFSGSKSGT SASLAISGLA SEDEADYICA AWDSSLNSWV FGGGKTLTVL GQPKAAPSVT 120
LFPPSSSEELQ ANKATLVCLI SDFYPGAVTV AWKADSSPVK AGVETTTPSK QSNNKYAASS 180
YLSLTPEQWK SHRSYSCQVT HEGSTVEKTV APTECS 216

```

```

SEQ ID NO: 444      moltype = AA length = 441
FEATURE           Location/Qualifiers
source           1..441
                 mol_type = protein
                 organism = Synthetic construct

```

```

SEQUENCE: 444
DVQLVESGGG LVQPGGSLRL SCAASGFTFD ISAMSWVRQA PGKGLEWVST ISGSAYSTYY 60
ADSVKGRFTI SRDNSKSTLY LQMNSLRAED TAVYYCAREI FSDYWGGLTL VTVSSASTKG 120
PSVFPPLAPCS RSTSESTAAL GCLVKDYFPE PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL 180
SSVTVPSSTL LGTKTYTCNV DHKPSNTKVD KRVESKYGPP CPPCPAPEFL GGPSVFLPPP 240
KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NRYVDGVEVH NAKTKPREEQ FNSTYRVVSV 300
LTVLHQDWLW GKEYKCKVSN KGLPSSIEKT ISKAKGQPRE PQVYTLPPSQ EEMTKNQVSL 360
TCLVKGFPYS DIAVEWESNG QPENNYKTTT PVLDSGDSFF LYSRLTVDKS RWQEGNVFSC 420
SVMHEALHNNH YTQKSLSLSL G 441

```

```

SEQ ID NO: 445      moltype = AA length = 216
FEATURE           Location/Qualifiers
source           1..216
                 mol_type = protein
                 organism = Synthetic construct

```

```

SEQUENCE: 445
QSVLTQPPSA SGTGQQRVTI SCSSGNSNIG RESVYVYQQL PGTAPKLLIY SNVQRPSGVP 60
DRFSGSKSGT SASLAISGLQ SEDEADYICG TWDDSLNGWV FGGGKTLTVL GQPKAAPSVT 120
LFPPSSSEELQ ANKATLVCLI SDFYPGAVTV AWKADSSPVK AGVETTTPSK QSNNKYAASS 180
YLSLTPEQWK SHRSYSCQVT HEGSTVEKTV APTECS 216

```

```

SEQ ID NO: 446      moltype = AA length = 440
FEATURE           Location/Qualifiers
source           1..440
                 mol_type = protein
                 organism = Synthetic construct

```

```

SEQUENCE: 446

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| | | | | | | |
|------------|------------|------------|------------|------------|------------|-----|
| DSLVESEGGL | VQPGGSLRLS | CAASGTFDI | SAMSWRQAP | GKGLEWVSTI | SGSAYSTYYA | 60 |
| DSVKGRFTIS | RDNSKSTLYL | QMNSLRAEDT | AVYYCAREIF | SDYWGLGLTV | TVSSASTKGP | 120 |
| SVFPLAPCSR | STSESTAALG | CLVKDYFPEP | VTVSWNSGAL | TSGVHTFPFV | LQSSGLYSLS | 180 |
| SVVTVPSSSL | GTKTYTCNVD | HKPSNTKVDK | RVESKYGPPC | PPCPAPEFLG | GPSVFLFPPK | 240 |
| PKDTLMISRT | PEVTCVVVDV | SQEDPEVQFN | WYVDGVEVHN | AKTKPREEQF | NSTYRVVSVL | 300 |
| TVLHQDWLNG | KEYKCKVSNK | GLPSSIEKTI | SKAKGQPREP | QVYTLPPSQE | EMTKNQVSLT | 360 |
| CLVKGFYPSD | IAVEWESNGQ | PENNYKTPP | VLDSGGSFPL | YSRLTVDKSR | WQEGNVFSCS | 420 |
| VMHEALHNHY | TQKLSLSLSL | | | | | 440 |

SEQ ID NO: 447 moltype = AA length = 216
 FEATURE Location/Qualifiers
 source 1..216
 mol_type = protein
 organism = Synthetic construct

| | | | | | | |
|---------------|------------|------------|------------|------------|------------|-----|
| SEQUENCE: 447 | | | | | | |
| QSVLTQPPSA | SGTPGQRVTI | SCSGSTSNIG | RESVYVYQQL | PGTAPKLLIY | LNSQRPSGVP | 60 |
| DRFSGSKSGT | SASLAISGLQ | SEDVADYYCG | TWDDSLNGWV | FGGGTKLTVL | GQPKAAPSVT | 120 |
| LFPSSSEELQ | ANKATLVCLI | SDFYPGAVTV | AWKADSSPVK | AGVETTTPSK | QSNKYAASS | 180 |
| YLSLTPEQWK | SHRSYSQVTV | HEGSTVEKTV | APTECS | | | 216 |

SEQ ID NO: 448 moltype = DNA length = 6765
 FEATURE Location/Qualifiers
 source 1..6765
 mol_type = other DNA
 organism = Synthetic construct

| | | | | | | |
|---------------|-------------|-------------|-------------|-------------|-------------|------|
| SEQUENCE: 448 | | | | | | |
| aacaaaat | taacgcttac | aatttccatt | cgccattcag | gctgcgcaac | tgttgggaag | 60 |
| ggcgatcgg | tcgggcctct | tcgctattac | gccagctggc | gaaaggggga | tgtgctgcaa | 120 |
| ggcgattaa | gtgggtaacg | ccagggtttt | cccagtcacg | acgttgtaaa | acgacggcca | 180 |
| gtgccaaag | gatcataaca | ttgaatcaat | attggcaatt | agccatatta | gtcattgggt | 240 |
| atatagcata | aatcaatatt | ggctattggc | cattgcatac | gttgatctca | tatcataata | 300 |
| tgtacattta | tattggctca | tgccaatat | gaccgccatg | ttgacattga | ttattgacta | 360 |
| gttattaata | gtaatacaat | acggggtcac | tagttccatg | cccataatag | gagttccgcg | 420 |
| ttacataaact | tacggtaaat | ggcccgcctg | gctgaccgcc | caacgacccc | cgccatttga | 480 |
| cgtaataat | gacgatgttt | cccatagtaa | cgccaatagg | gactttccat | tgacgtcaat | 540 |
| gggtggagta | tttacggtaa | actgcccaact | tggcagtaga | tcaagtgtag | catatgcca | 600 |
| gtccgcccoc | tattgacgtc | aatgacggta | aatggcccgc | ctggcattat | gccagtaga | 660 |
| tgaccttaag | ggactttcct | acttggcagt | acatctacgt | attagtcac | gctattacca | 720 |
| tggtgatgag | gttttggcag | tacaccaatg | ggcgtggata | gcggtttgac | tcacggggat | 780 |
| ttccaagtct | ccaccocatt | gacgtcaatg | ggagtttggt | ttggcaccga | aatcaacggg | 840 |
| actttccaaa | atgtcgtaat | aaccccgcct | cgttgacgca | aatggggcgt | aggcgtgtac | 900 |
| gggtggaggt | ctatataaag | agagctcgtt | tagtgaaccg | tcagaatttt | gtaatacgac | 960 |
| tcactatagg | gcgcccggga | attcgtogac | tggatccggt | accgaggaga | ctgcccgcg | 1020 |
| cgatcgccgg | cgccgacagat | ctcaagctta | tggacatgag | gggtccagca | caactctctg | 1080 |
| gattactatt | gttatggctg | cgaggtgccc | gctgttatcc | ttacgacgtg | cctgactacg | 1140 |
| ccccaggatg | gttctcagct | tccccagaga | ggccctggaa | cgccccacc | ttctcccag | 1200 |
| ccctgctcct | ggtgaccgaa | ggggacaacg | ccacctteac | ctgcagcttc | tccaacgcat | 1260 |
| cgagagactt | cggtctaaac | ttgtacagga | tgagcccag | caaccagagc | gacaactctg | 1320 |
| ccgctctccc | cgaggaccgc | agccagcccg | gccaggactg | ccgcttccgt | gtcacacgct | 1380 |
| tgcccaacgg | gctgacttcc | cacatgagcg | tggtcagggc | ccggcgcaat | gacagcggca | 1440 |
| cctacctctg | tggggccatc | tccttggccc | ccaaggcgca | gatcaaaag | agcctgctgg | 1500 |
| cagagctcag | ggtgacagag | aaagggcgag | aagtgcccaac | agcccaccoc | agcccctcac | 1560 |
| ccaggccacg | cggccagttc | caagccctgg | tggttgggtg | cggtggcgcc | ctgctgggca | 1620 |
| gcctggctg | gctagtctgg | gtcctggccc | tcatctgtct | ccgcccgcga | caagggacaa | 1680 |
| tagaagccag | tcgcaacctg | cgcttaagc | ggccgcactc | gaggtttaa | cgccggcgcc | 1740 |
| cggtcatagc | ttgttcttga | acagatcccg | ggtggcatcc | ctgtgacccc | tccccagtgc | 1800 |
| ctctcctggc | cctggaagtt | gccactccag | tgccaccacg | ccttgcctca | ataaaatata | 1860 |
| gttgcatcat | ttgtctgac | taggtgtcct | tctataaat | tatggggtgg | aggggggtgg | 1920 |
| tatggagcaa | ggggcaagtt | gggaagacaa | cctgtagggc | ctgcccgggtc | tattgggaac | 1980 |
| caagctggag | tgcagtgcca | caatcttggc | tcaactgcaat | ctcccgcctcc | tggttccaag | 2040 |
| cgattctcct | gcctcagcct | cccagtttgt | tgggattcca | ggcatgcatg | accaggctca | 2100 |
| gctaattttt | gttttttttg | tagagacggg | gtttcaccat | attggccagg | ctggtctcca | 2160 |
| actcctaact | tcaggtgac | taccacactt | ggcctcccaa | attgctggga | ttacagggcgt | 2220 |
| gaaccactgc | tcctctccct | gtcctcttga | ttttaaata | actataccag | caggaggagc | 2280 |
| tccagacaca | gcataggcta | cctggccatg | cccaaccggt | gggacatttg | agttgcttgc | 2340 |
| ttggcaactg | cctctcatgc | gttgggtcca | ctcagtagat | gcctgtttaa | ttgggtacgc | 2400 |
| ggccagcttg | gctgtggaat | gtgtgtcagt | tagggtgtgg | aaagtcacca | ggctccccag | 2460 |
| caggcagaag | tatgcaaaag | atgcatctca | attagttagc | aaccaggtgt | ggaaaagccc | 2520 |
| caggctcccc | agcaggcaga | agtatgcaaa | gcatgcatct | caattagtag | gcaaccatag | 2580 |
| tcccggccct | aactcccgcc | atcccggccc | taactccgcc | cagttccgcc | cattctccgc | 2640 |
| ccccggctg | actaattttt | tttatttatg | cagaggccga | ggccgcccctg | gcctctgagc | 2700 |
| tattccagaa | gtagttagga | ggcttttttg | gaggcctagg | cttttgcaaa | aaagctcccg | 2760 |
| gagcttgat | atccattttc | ggatctgac | aagagacacg | tacgacctag | aaaaagcctg | 2820 |
| aactcaccgc | cagctctggt | gagaagtttc | tgatcgaaaa | ggtcgacagc | gtctccgacc | 2880 |
| tgatgcagct | ctcggagggc | gaagaatctc | gtgctttcag | cttgcagtag | ggagggcgtg | 2940 |
| gatatgtcct | gcccggtaaat | agctgcgccc | atggtttcta | caaagatcgt | tatggttatc | 3000 |
| ggcaacttgc | atcggcccgc | ctcccgatcc | cggaagtgtc | tgacattggg | gaatttagcg | 3060 |
| agagcctgac | ctattgcatc | tcccgcctg | cacaggggtg | cacgttgcaa | gacctgctg | 3120 |
| aaaccgaact | gcccgcctgt | ctgcaaccgg | tcgcccggagc | catggatgca | atcgtctcgg | 3180 |

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ccgatccttag ccagacgagc gggttcggcc cattcggacc gcaaggaatc ggtcaataca 3240
ctacatggcg tgatttccata tgcgcgattg ctgatcccca tegtatcac tggcaaaactg 3300
tgatggagca caccgtcagt gcgtccgtcg cgcaggctct cgatgagctg atgctttggg 3360
ccgaggactg ccccgaaagc cggcacctcg tgcacgcgga tttcggetcc aacaatgtcc 3420
tgacggacaa tggccgcata acagcggtea ttgactggag cgaggcgatg ttcggggatt 3480
cccaatacga ggtcgccaac atcttcttct ggaggccgtg gttggcttgt atggagcagc 3540
agacgcgcta cttcgagcgg aggcacccgg agcttgcagg atcgcccgcg ctccgggctg 3600
atatgctccg catttggtctt gaccaactct atcagagctt ggttgacggc aatttcgatg 3660
atgcagcttg ggcgcagggg cgatgcgacg caatcgtccg atccggagcc gggactgtcg 3720
ggcgtacaca aatcgcccgc agaagcgcgg ccgtctggac cgatggctgt gtagaagtac 3780
tcgcccgatg tggaaaccga cgcgccagca ctcgtccgag ggcaaaaggaa tagctgcagc 3840
gggactctgg ggttcogaat gaccgaccaa cgcagcgcga acctgccatc acgagatctc 3900
gattccacog cccgctctca tgaagggtg ggcttcggaa tcgthttccg ggaocgccc 3960
tggatgatcc tccagcggcg ggatctcatg ctggagttct tcgcccaccc caacttgtht 4020
attgcagctt ataatgggta caataaaagc aatagcatca caaatctcac aaataaagca 4080
tttttttccac tgcattctag ttgtggtht tccaaactca tcaatgtatc ttatcatgtc 4140
tगतataccgt gcacctctag cttagacttg gcgtaatcat ggtcatagct gtttccctgtg 4200
tgaaatgttt atccgctcac aatccacac aacatcagag ccggaagcat aaagtgtaaa 4260
gcttggggtg ctaaatgagt gagtaactc acattaatg cgttgcgctc actgcccgtc 4320
ttccagtcgg gaaacctgtc gtgccagctg cattaatgaa tcggccaacg cgcggggaga 4380
ggcggthtgc gtattggggc ctcttccgct tctctgctca ctgactcgct gcgctcggctc 4440
gttcggctgc ggcgagcggg atcagctcac tcaaaggcgg taatacggth atccacagaa 4500
tcaggggata acgcaggaaa gaacatgtga gcaaaaggcc agcaaaaggc caggaaccgt 4560
aaaaaggccg cgttgcggcg gthtttccat aggctccgcc cccctgcagca gcatcacaaa 4620
aatcgacgct caagtccagag gtggcgaaac ccgacaggac tataagata ccaggcgttt 4680
ccccctggaa gctccctcgt gcgctctcct gttccgaccc tgcgcttac cggataacctg 4740
tccgcttctc tcccttcggg aagcgtggcg cthttccata gctcacgctg taggtatctc 4800
agthcgggtg agtgcgtctg ctccaagctg ggctgtgtgc acgaaccccc cgttcagccc 4860
gaccgctcgg ccttatccgg taactatcgt cttgagthca acccgtaag acacgactta 4920
tcgcccactgg cagcagccac tggtaacagg attagcagag cgaggatagt aggcggtgct 4980
acagagthct tgaagthggt gcctaactac ggctacacta gaagaacagt atthggtatc 5040
tgcgctctgc tgaagcagth tactctccga aaaagagthg gtagctcttg atccggcaaa 5100
caaacaccog ctgthgagcg thgtthtttt gthttgcaagc agcagatthc gcgcagaaaa 5160
aaaggatctc aagaagatcc thgtatctt tctacggggg ctgacgctca gthgaaagaa 5220
aactcacgth aagggattht gthcatgaga thatacaaaa gthctctcac ctagatcctt 5280
thaaatthaa aatgaagtht thaatcaatc thaaagthata atgagthaac thggtctgac 5340
agthaccaat gctthaatcag thaggcacct atctcagcga thctgctatth thgttcatcc 5400
atagthgctt gactccccgt cgtgtagata actacgatac gggaggthct accatctggc 5460
cccagthctg caatgatacc gcgagaccca cgtcaccggt ctccagatth atcagcaata 5520
aaccagccag ccggaaggcg cgaagcgaaga agthgthctg caactthatc cgcctccatc 5580
cagthctatta atthgtccg ggaagctaga gthaaagtht cgcagthtaa tagthttgcg 5640
aacgthgttg ccatthctac aggcathctg thgtcacgct cgtcgtthtg thgtgthtca 5700
thcagthccg gthtcccaag atcaaggcga thtcatgath cccccatgth gthgcaaaaa 5760
gcgthtagct ccttcggthc tccgathctt gthcagaagth agthggccgc agthgthata 5820
ctcatgthta thgcagcact gcataatthct cthactgthca thgcatcctg aagathctth 5880
thctgthactg thtgaactca aaccaagthca thctgagaath agthgthctg gcgacagagth 5940
thctctthgc gthgctcaat acgggthaat accgthccac atagcagaac ththaaagthg 6000
ctcatcathg gaaaaagthct thcgggthcga aaactctcaa gthctctcac gctgthgaga 6060
thcagthtca thtaaccacc cgtgthcacc aactgathct cagathctth thactthcacc 6120
agcgtthctg gthgagcaaa aacaggaag caaaaagthc caaaaaagthg aataagthgcg 6180
acagthaaat gthgataact cactactctc cthththcaat athatgthag cththtcatg 6240
gththattgtc thctgagcgg atacaththt gaathgthatt agaaaaataa acaathagthg 6300
gthtccgthca cththtcccg aaaaagthcga cctgacgthc cctgthagcgg cgcathaaagc 6360
gthcgggthg thgtgthtcc gcgacgctg accgthcac thtccagcgc cctagcggcc 6420
gthctctthc gthtcttccc thctcttctc gccagthtcc cggctthtcc cgtcaagct 6480
ctaaatcggg gthctccctth agggthtccga thtagthctt thcggcacct cgaacccaaa 6540
aaactgath agggthgag thcagthagth gggccactgc cctgathagc gththtctcg 6600
cctthgacgt thgagthctg thctthtaat agthgactct thtccaaaac thgaaacaaca 6660
ctcaaccctc thctcggthca thctththgath thataagthg ththtgcgath thcggctat 6720
thgthtaaaaa atgagthgath thaaacaaaa thtaacgthca attht 6765

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SEQ ID NO: 449 moltype = AA length = 447
FEATURE Location/Qualifiers
source 1..447
mol_type = protein
organism = Synthetic construct

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SEQUENCE: 449
QVQLVQSGSE LKKPGASVKV SCKASGYTFT SYAMHWVRQA PQGLEWMGY ISPFTGRATY 60
AQQFTGRFVF SLDTSVSTAY LQISSLKAED TAVYYCARDY DYRYYYAMDY WGGQTTVTVS 120
SASTKGPSVF PLAPCSRSTS ESTAALGLCV KDYPPEPVTV SWNSGALTSV VHTFPAVLQS 180
SGLYSLSSVV TVPSSSLGTK TYTCNVDPKPK SNTKVDKRVV SKYGPFPFPP PAPEFLGGPS 240
VFLFPPKPKD TLMISRTPEV TCVVVDVDSQE DPEVQFNWYV DGEVHNAKT KPREEQFNST 300
YRVVSVLTVL HQDWLNKEY KCKVSNKGLP SSIETISKAK KGQPREPQVY TLPSSQEEMT 360
KNQVSLTCLV KGFYPSDIAV EWESNGQPEN NYKTTTPVLD SDGSFPLYSR LTVDKSRWQE 420
GNVFSQSVMH EALHNYTQK SLSLSLG 447

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SEQ ID NO: 450 moltype = AA length = 215
FEATURE Location/Qualifiers
source 1..215

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mol_type = protein
organism = Synthetic construct

SEQUENCE: 450
EIVLTQSPDF QSVTPKEKVT ITCRASQSIP PQFLHWYQQK PDQSPKLLIK AASQRASGVP 60
SRFSGSGSGT DFTLTINSLE ABDAATYYCH QFHSSPLTFG GGTKLEIKRT VAAPSVFIFP 120
PSDEQLKSGT ASVVCLLNMF YPREAKVQWK VDNALQSGNS QESVTEQDSK DSTYLSLSTL 180
TLKADYKHKV KYACEVTHQ GLSSPVTKSF NRGEC 215

SEQ ID NO: 451      moltype = AA length = 579
FEATURE           Location/Qualifiers
source           1..579
                 mol_type = protein
                 organism = Synthetic construct

SEQUENCE: 451
QVQLVESGGG VVQPGRSLRL DCKASGITFS NSGMHWVRQA PGKGLEWVAV IWYDGSKRY 60
ADSVKGRFTI SRDNSKNTLF LQMNSLRAED TAVYYCATND DYWGQGLVLT VSSASTKGPS 120
VFPLAPCSRST TSESTAALGC LVKDYFPEPV TVSWNSGALT SGVHTFPAVL QSSGLYSLSS 180
VITVPSSTLG TKTYTCNVDH KPSNTKVDKR VESKYGPPCP PCPAPPELGG PSVFLPPPKP 240
KDTLMSRTP EYVTCVVDVVS QEDPEVQFNW YVDGVEVHNA KTKPREEQFN STYRVVSLT 300
VLHQDWLNGK EYKCKVSNKG LPSSIEKTIS KAKGQPREPQ VYTLPPSQEE MTKNQVSLT 360
LVKGFYPSDI AVEWESNGQP ENNYKTTTPV LDSDGSFPLY SRLTVDKSRW QEGNVFSCSV 420
MHEALHNYHT QKSLSLSLGK SGGGSAPTSS SSTKKTQLQL EHLALLQMI LNGINNYKNP 480
KLTEMLTKFK YMPKATELKH LQCLEEELK PLEEVNLQAQ SKNFHLRPRD LISNINIVL 540
ELKGETTFM CEYADETATI VEFLNRWITF CQSIISTLT 579

SEQ ID NO: 452      moltype = AA length = 214
FEATURE           Location/Qualifiers
source           1..214
                 mol_type = protein
                 organism = Synthetic construct

SEQUENCE: 452
EIVLTQSPAT LSLSPGERAT LSCRASQSVS SYLAWYQQKP GQAPRLLIYD ASNRATGIPA 60
RFGSGSGGTD FTLTISLLEP EDFAVYYCQQ SSNWPRTPGQ GTKVEIKRTV AAPSVFIFPP 120
SDEQLKSGTA SVVCLLNMFY PREAKVQWKV DNALQSGNSQ ESVTEQDSK DSTYLSLSTL 180
LSKADYKHKV VYACEVTHQ LSSPVTKSFN RGEC 214

SEQ ID NO: 453      moltype = AA length = 588
FEATURE           Location/Qualifiers
source           1..588
                 mol_type = protein
                 organism = Synthetic construct

SEQUENCE: 453
EVQLLESGGG LVQPGGSLRL SCAASGFTFS SNYMSWVRQA PGKGLEWVSA ISSSGGTIFY 60
ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAKHK WNAVYYDGMV VWGQGTITVTV 120
SSASTKGPSV FPLAPCSRST SESTAALGCL VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ 180
SSGLYSLSSV VITVPSSTLGT KTYTCNVNDHK PSNTKVDKRV ESKYGPCCP CPAPPELGGP 240
SVFLPPPKPK DTLMSRTP EYVTCVVDVVSQ EDPEVQFNWY VDGVEVHNAK TKPREEQFNS 300
TYRVVSVLTV LHQDWLNGKE YKCKVSNKGL PSSIEKTISK AKGQPREPQV YTLPPSQEEM 360
TKNQVSLTCL VKGFYPSDIA VEWESNGQPE NNYKTTTPVL DSDGSFPLY RLTVDKSRWQ 420
EGNVFSCSVM HEALHNYHTQ KSLSLSLGKS GGGGSAPTSS STKKTQLQLE HLLALLQMI 480
NGINNYKNPK LTEMLTKFKY MPKATELKH LQCLEEELK PLEEVNLQAQ KNFHLRPRDL 540
ISNINIVILE LKGETTFMCEYADETATIV EFLNRWITFC QSIISTLT 588

SEQ ID NO: 454      moltype = AA length = 585
FEATURE           Location/Qualifiers
source           1..585
                 mol_type = protein
                 organism = Synthetic construct

SEQUENCE: 454
EVQLLESGGG LVQPGGSLRL SCTASGFTFS SYEMQWVRQA PGKGLEWVLA ITSSSHIFY 60
ADSVKGRFTV SRDNSKNTLY LQMNSLRAED TAVYYCTKDL NSYYGLDVGW QGTTVTVSSA 120
STKGPSVFPPL APCSRSTSES TAALGCLVKD YFPEPVTVSW NSGALTSGVH TFPVAVLQSSG 180
LYSLSSVTV PSSSLGKTY TCNVNDHKPSN TKVDKRVESK YGPPCCPPCA PEPFLGGPSVF 240
LFPKPKDTL MISRTPEVTC VVVDVSDQEDP EVQFNWYVDG VEVHNAKTKP REEQFNSTYR 300
VVSVLTVLHQ DWLNGKEYKC KVSNGKLPSS IEKTISKAKG QPREPQVYTL PPSQEEEMTKN 360
QVSLTCLVKG FYPYSDIAVEW ESNQGPENNY KTTTPVLDSD GSPFLYSRLT VDKSRWQEGN 420
VFSCVMHEA LHNHYTQKSL SLSLGSKGGG GSAPTSSSTK KTQLQLEHLH LALQMIHLNGI 480
NNYKNPKLTE MLTKFKYMPK KATELKHLCQ LEEELKPLEE VLNLAQSKNF HLRPRDLISN 540
INVIVLELKG SETTFMCEYADETATIVEFL NRWITFCQSI ISTLT 585

SEQ ID NO: 455      moltype = AA length = 588
FEATURE           Location/Qualifiers
source           1..588
                 mol_type = protein
                 organism = Synthetic construct

SEQUENCE: 455
EVQLLESGGG LVQPGGSLRL SCAASGFTFS DYMSWVRQA PGKGLEWVSA ISSSGGTIFY 60
ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAKHK WNDVYDAMD VWGQGTITVTV 120
SSASTKGPSV FPLAPCSRST SESTAALGCL VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ 180

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SSGLYSLSSV VTPVSSSLGT KTYTCNVDPK PSNTKVDKRV ESKYGPPCPP CPAPEFLGGP 240
SVFLFPPKPK DTLMISRTPV VTCVVVDVVSQ EDPEVQFNWY VDGVEVHNAK TKPREEQFNS 300
TYRVVSVLTV LHQDWLNGKE YKCKVSNKGL PSSIEKTISK AKGQPREPQV YTLPPSQEEM 360
TKNQVSLTCL VKGFYPSDIA VEWESNGQPE NNYKTTPPVL DSDGSFFLYS RLTVDKSRWQ 420
EGNVFSCSVM HEALHNHYTQ KSLSLSLGKS GGGGSAPTSS STKKTQLQLE HLLALQML 480
NGINNYKNPK LTEMPTFKFY MPKKATELKH LQCLEEELKP LEEVLNLAQS KNFHLRPRDL 540
ISININVIVLE LKGSSETFMC EYADETATIV EFLNRWITFC QSIISTLT 588

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SEQ ID NO: 456      moltype = AA length = 575
FEATURE           Location/Qualifiers
source            1..575
                  mol_type = protein
                  organism = Synthetic construct

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SEQUENCE: 456
DVQLVESGGG LVQPGGSLRL SCAASGFTFD ISAMSWVRQA PGKGLEWVST ISGSAYSTYY 60
ADSVKGRFTI SRDNSKSTLY LQMNSLRAED TAVYYCAREI FSDYVGLGTL VTVSSASTKG 120
PSVFLAPCS RSTSESTAAL GCLVKDYFPE PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL 180
SSVTVPSSS LGTKTYTCNV DHKPSNTKVD KRVESKYGPP CPPCPAPEFL GGPSVFLFPP 240
KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NNYVDGVEVH NAKTKPREEQ FNSTYRVVSV 300
LTVLHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQPRE PQVYTLPPSQ EEMTKNQVSL 360
TCLVKGFPYS DIAVEWESNG QPENNYKTPP PVLDSGDSFF LYSRLTVDKS RWQEGNVFSC 420
SVMHEALHNH YTKLSLSLGL KAPTSSSTK KTQLQLEHLL LALQMLNGI NNYKNPKLTE 480
MLTFKFPYMPK KATELKHLCQ LBEELKPLEE VLNLAQSKNF HLRPRDLISN INVIVLELKG 540
SETTFMCEYA DETATIVEEFL NRWITFCQSI ISTLT 575

```

```

SEQ ID NO: 457      moltype = AA length = 574
FEATURE           Location/Qualifiers
source            1..574
                  mol_type = protein
                  organism = Synthetic construct

```

```

SEQUENCE: 457
DSLVESGGGL VQPGGSLRLS CAASGFTFDI SAMSWVRQAP GKGLEWVSTI SGSAYSTYYA 60
DSVKGRFTIS RDNSKSTLYL QMNSLRAEDT AVYYCAREIF SDYVGLGTLV TVSSASTKGP 120
SVFPLAPCSR STSESTAALG CLVKDYFPEP VTVSWNSGAL TSGVHTFPAV LQSSGLYSL 180
SVVTVPSSSL GTKTYTCNVD HKPSNTKVDK RVESKYGPPC PPCPAPEFLG GPSVFLFPPK 240
PKDTLMISR TPEVTCVVVD VSQEDPEVQFN WYVDGVEVHN AKTKPREEQF NSTYRVVSVL 300
TVLHQDWLNG KEYKCKVSNK GLPSSIEKTI SKAKGQPREP QVYTLPPSQ EMTKNQVSLT 360
CLVKGFPYPS DIAVEWESNG PENNYKTPP VLDSGDSFFL YSRLTVDKSR WQEGNVFSCS 420
VMHEALHNHY TQKLSLSLGL KAPTSSSTK TQLQLEHLL ALQMLNGIN NYKNPKLTEM 480
LTFKFPYMPK ATELKHLQCL EELKPLEEV LNLQSKNFH LRPDLISNI NVIVLELKG 540
ETTFMCEYAD ETATIVEEFLN RWITFCQSI STLT 574

```

```

SEQ ID NO: 458      moltype = AA length = 448
FEATURE           Location/Qualifiers
source            1..448
                  mol_type = protein
                  organism = Synthetic construct

```

```

SEQUENCE: 458
EVQLLES GGG LVQPGGSLRL SCAASGFTFK DYCMTWVRQA PGKGLEWVSA IVYSGGSTYY 60
ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAKYT RASYFYDAMD VWGQGTITVTV 120
SSASTKGPSV FPLAPCSRST SESTAALGCL VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ 180
SSGLYSLSSV VTPVSSSLGT KTYTCNVDPK PSNTKVDKRV ESKYGPPCPP CPAPEFEGGP 240
SVFLFPPKPK DTLMISRTPV VTCVVVDVVSQ EDPEVQFNWY VDGVEVHNAK TKPREEQFNS 300
TYRVVSVLTV LHQDWLNGKE YKCKVSNKGL PSSIEKTISK AKGQPREPQV YTLPPSQEEM 360
TKNQVSLTCL VKGFYPSDIA VEWESNGQPE NNYKTTPPVL DSDGSFFLYS RLTVDKSRWQ 420
EGNVFSCSVM HEALHNHYTQ KSLSLSLG 448

```

```

SEQ ID NO: 459      moltype = AA length = 448
FEATURE           Location/Qualifiers
source            1..448
                  mol_type = protein
                  organism = Synthetic construct

```

```

SEQUENCE: 459
EVQLLES GGG LVQPGGSLRL SCAASGFTFK DYCMTWVRQA PGKGLEWVSA IVYSGGSTYY 60
ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAKYT RASYFYDAMD VWGQGTITVTV 120
SSASTKGPSV FPLAPCSRST SESTAALGCL VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ 180
SSGLYSLSSV VTPVSSSLGT KTYTCNVDPK PSNTKVDKRV ESKYGPPCPP CPAPEFAGAP 240
SVFLFPPKPK DTLMISRTPV VTCVVVDVVSQ EDPEVQFNWY VDGVEVHNAK TKPREEQFNS 300
TYRVVSVLTV LHQDWLNGKE YKCKVSNKGL PSSIEKTISK AKGQPREPQV YTLPPSQEEM 360
TKNQVSLTCL VKGFYPSDIA VEWESNGQPE NNYKTTPPVL DSDGSFFLYS RLTVDKSRWQ 420
EGNVFSCSVM HEALHNHYTQ KSLSLSLG 448

```

```

SEQ ID NO: 460      moltype = AA length = 448
FEATURE           Location/Qualifiers
source            1..448
                  mol_type = protein
                  organism = Synthetic construct

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```

SEQUENCE: 460
EVQLLES GGG LVQPGGSLRL SCAASGFTFS DYMSWVRQA PGKGLEWVSA ISSSGGTIFY 60

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ADSVKGRFII SRDNSKNTLY LQMNSLRAED TAVYYCAKHK WNDVYYDAMD VWGQGTFTVTV 120
SSASTKGPSV FPLAPCSRST SESTAALGCL VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ 180
SSGLYSLSSV VTPSSSLGT KTYTCNVDPK PSNTKVDKRV ESKYGPCCPP CPAPEFLGGP 240
SVFLFPPKPK DTLMISRTP E VTCVVVDVSO EDPEVQFNWY VDGVEVHNAK TKPREEQFNS 300
TYRVVSVLTV LHQDNLNGKE YKCKVSNKGL PSSIEKTISK AKGQPREPQV YTLPPSQEEM 360
TKNQVSLTCL VKGFYPSDIA VEWESNGQPE NNYKTTTPVL DSDGSFFLYS RLTVDKSRWQ 420
EGNVFSCSVM HEALHNYHTQ KSLSLSLG 448

```

```

SEQ ID NO: 461      moltype = AA length = 441
FEATURE           Location/Qualifiers
source           1..441
                 mol_type = protein
                 organism = Synthetic construct

```

```

SEQUENCE: 461
DMQLVESGGG VVRPGESLRL SCTASGFTFS ISAMSWVRQA PGKGLEWVSA ISGTAYSTYY 60
ADSVRGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAKDN FFDYWGLGTL VTVSSASTKG 120
PSVFLAPCS RSTSESTAAL GCLVKDYFPE PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL 180
SSVTVPSSS LGTKTYTCNV DHKPSNTKVD KRVEKYGPP CPPCPAPEFL GGPSVFLFPP 240
KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NQYVDGVEVH NAKTKPREEQ FNSTYRVVSV 300
LTVLHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQPRE PQVYTLPPSQ EEMTKNQVSL 360
TCLVKGFPYS DIAVEWESNG QPENNYKTTT PVLDSDGSPF LYSRLTVDKS RWQEGNVFSC 420
SVMHEALHNN YTQKSLSLSL G 441

```

```

SEQ ID NO: 462      moltype = AA length = 216
FEATURE           Location/Qualifiers
source           1..216
                 mol_type = protein
                 organism = Synthetic construct

```

```

SEQUENCE: 462
QSVMTQPPSA SGTGQQRVTI SCSGVTSNIG SNSVYVYQQL PGTAPKLLIY LNSQRPSGVV 60
DRFSGSKSGT SASLAISGLQ SEDEADYYCG TWDDSLNGWV FGGTKLTVL GQPKAAPSVT 120
LPPPSSEELQ ANKATLVCLI SDFYPGAVTV AWKADSSPVK AGVETTTPSK QSNKYAASS 180
YLSLTPEQWK SHRSYSQVVT HEGSTVEKTV APTECS 216

```

```

SEQ ID NO: 463      moltype = AA length = 441
FEATURE           Location/Qualifiers
source           1..441
                 mol_type = protein
                 organism = Synthetic construct

```

```

SEQUENCE: 463
DVQLVESGGG VVRPGESLRL SCTASGFTFS ISAMSWVRQA PGKGLEWVSA ISGTAYSTYY 60
ADSVRGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAKDN FFDYWGLGTL VTVSSASTKG 120
PSVFLAPCS RSTSESTAAL GCLVKDYFPE PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL 180
SSVTVPSSS LGTKTYTCNV DHKPSNTKVD KRVEKYGPP CPPCPAPEFL GGPSVFLFPP 240
KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NQYVDGVEVH NAKTKPREEQ FNSTYRVVSV 300
LTVLHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQPRE PQVYTLPPSQ EEMTKNQVSL 360
TCLVKGFPYS DIAVEWESNG QPENNYKTTT PVLDSDGSPF LYSRLTVDKS RWQEGNVFSC 420
SVMHEALHNN YTQKSLSLSL G 441

```

```

SEQ ID NO: 464      moltype = AA length = 441
FEATURE           Location/Qualifiers
source           1..441
                 mol_type = protein
                 organism = Synthetic construct

```

```

SEQUENCE: 464
DVQLVESGGG VVRPGESLRL SCAASGFTFS IYAMSWVRQA PEGGLEWVSH ISASGGSTYY 60
ADSVKGRFAI SRDNSKNTLY LQMNSLRAED TAVYYCTTNL GSDYWGLGTL VTVSSASTKG 120
PSVFLAPCS RSTSESTAAL GCLVKDYFPE PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL 180
SSVTVPSSS LGTKTYTCNV DHKPSNTKVD KRVEKYGPP CPPCPAPEFL GGPSVFLFPP 240
KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NQYVDGVEVH NAKTKPREEQ FNSTYRVVSV 300
LTVLHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQPRE PQVYTLPPSQ EEMTKNQVSL 360
TCLVKGFPYS DIAVEWESNG QPENNYKTTT PVLDSDGSPF LYSRLTVDKS RWQEGNVFSC 420
SVMHEALHNN YTQKSLSLSL G 441

```

```

SEQ ID NO: 465      moltype = AA length = 441
FEATURE           Location/Qualifiers
source           1..441
                 mol_type = protein
                 organism = Synthetic construct

```

```

SEQUENCE: 465
DVQLVESGGG VVRPGESLRL SCAASGFTFS IYAVSWVRQA PEGGLEWVSH ISASGGSTYY 60
ADSVKGRFAI SRDNSKNTLY LQMNSLRAED TAVYYCTTNL GSDYWGLGTL VTVSSASTKG 120
PSVFLAPCS RSTSESTAAL GCLVKDYFPE PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL 180
SSVTVPSSS LGTKTYTCNV DHKPSNTKVD KRVEKYGPP CPPCPAPEFL GGPSVFLFPP 240
KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NQYVDGVEVH NAKTKPREEQ FNSTYRVVSV 300
LTVLHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQPRE PQVYTLPPSQ EEMTKNQVSL 360
TCLVKGFPYS DIAVEWESNG QPENNYKTTT PVLDSDGSPF LYSRLTVDKS RWQEGNVFSC 420
SVMHEALHNN YTQKSLSLSL G 441

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-continued

SEQ ID NO: 466 moltype = AA length = 216
FEATURE Location/Qualifiers
source 1..216
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 466
QSVLTQPPSA SGTGQQRVTI SCSGYSYSDIG TNYVYVYQQQL PGTAPKLLIF ATDRRPSGVP 60
DRFSGSKSGT SASLAISGLQ SEDEADYYCG TWDDSLNVWV FGGGKLTVL GQPKAAPSVT 120
LPPSSSEELQ ANKATLVCLI SDFYPGAVTV AWKADSSPVK AGVETTTPSK QSNKYAASS 180
YLSLTPEQWK SHRSYSQVQT HEGSTVEKTV APTECS 216

SEQ ID NO: 467 moltype = AA length = 443
FEATURE Location/Qualifiers
source 1..443
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 467
DVQLVESGGG VVRPGESLRL SCAASGFTFS TDAMGWVQA PEGGLEWVSL ISGSGYSTYY 60
ADSVKGRFTI SRDNSKNTLY LQMNSLTAED TAVYYCAKNS LAFPDYWGLG TLVTVSSAST 120
KGPSVFPPLAP CSRSTSESTA ALGCLVKDYF PEPVTVSWNS GALTSGVHTF PAVLQSSGLY 180
SLSSVVTVPS SSLGKTYTC NVDHKPSNTK VDKRVESKYG PPCPPCPAPE FLGGSPVFLF 240
PKPKDITLMI SRTEVTCVVDVVSQEDPEV QFNWYVDGVE VHNAKTKPRE EQFNSTYRVV 300
SVLTVLHQDW LNGKEYKCKV SNKGLPSSIE KTISKAKGQP REPQVYTLPP SQEEMTKNQV 360
SLTCLVKGFY PSDIAVWES NGQPENNYKT TPPVLDSDGS FFLYSRLTVD KSRWQEGNVF 420
SCVMHEALH NHYTQKLSLSL SLG 443

SEQ ID NO: 468 moltype = AA length = 216
FEATURE Location/Qualifiers
source 1..216
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 468
QSVLTQPPSA SGTGQQRVTI SCSGGSSNIG RESVNWYQQQL PGTAPKLLIY STDRRPSGVP 60
DRFSGSKSGT SASLAISGLQ SEDEADYYCG TWDNDLNGWV FGGGKLTVL GQPKAAPSVT 120
LPPSSSEELQ ANKATLVCLI SDFYPGAVTV AWKADSSPVK AGVETTTPSK QSNKYAASS 180
YLSLTPEQWK SHRSYSQVQT HEGSTVEKTV APTECS 216

SEQ ID NO: 469 moltype = AA length = 449
FEATURE Location/Qualifiers
source 1..449
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 469
DVQLQESGPG LVKPSQSLSL TCTVTGHSIT SDYAWNWIRO PPGDKLEWVG YISYSGYTTY 60
NPSLKSRSVI TRDTSKNQFF LQLNSVTTED TATYPCARDL DYGPWFAYWG QGTLVTVSAA 120
STKGPSVFPL APSSKSTSGG TAALGCLVKD YFPEPVTVSW NSGALTSGVH TFPVAVLQSSG 180
LYSLSSVTVV PSSSLGTQTY ICNVNHNKPSN TKVDKKVEPK SCDKHTHTCP CPAPPELLGGP 240
SVFLFPPKPK DTLMISRTP VTCVVDVDSH EDPEVKFNWY VDGVEVHNMAK TKPREEQYNS 300
TYRVVSVLTV LHQDNLNGKE YKCKVSNKAL PAPIEKTISK AKGQPREPQV YTLPPSRDEL 360
TKNQVSLTCL VKGFPYPSDIA VEWESNGQPE NNYKTTTPVL DSDGSFFLYS KLTVDKSRWQ 420
QGNVFSQSVM HEALHNHYTQ KSLSLSPGK 449

SEQ ID NO: 470 moltype = AA length = 214
FEATURE Location/Qualifiers
source 1..214
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 470
DIQMTQSPAS LSASVGETVT LTCRASENIH NYLAWYQQKQ GKSPQLLVYN VKTLADGVPS 60
RFGSGSGTQ YSLKINSLQP EDFGSYQCQ FWSSPWTFGG GTKVEIKRVT AAPSPVIFPP 120
SDEQLKSGTA SVVCLLNNFY PREAKVQWKV DNALQSGNSQ ESVTEQDSKD STYLSSTLT 180
LSKADYEKHK VYACEVTHQG LSSPVTKSFN RGEC 214

SEQ ID NO: 471 moltype = AA length = 585
FEATURE Location/Qualifiers
source 1..585
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 471
EVQLLESGGG LVQPGGSLRL SCAASGFTFK DYCMTWVQA PGKGLEWVSA IVYSGGSTYY 60
ADSVKGRFTI SRDNSKNTLY LQMNNLRAED TAVYYCAKYT RASYFYDAMD VWGQGTITVTV 120
SSASTKGPSV FPLAPSSKST SGGTAALGCL VKDYFPEPVT VSWNSGALTS GVHTFPVAVLQ 180
SSGLYSLSSV VTPVSSSLGT QTYICNVNHNK PSNTKVDKVK EPKSCDKTHT CPPCPAPELA 240
GAPSVFLFPP KPKDTLMI SR TEPEVTCVVDV VSHEDPEVKF NWFYVDGVEVH NAKTKPREEQ 300
YNSTYRVVSV LTVLHQDWLN GKEYKCKVSN KALPAPIEKT ISKAKGQPRE PQVYTLPPSR 360
DELTKNQVSL TCLVKGFPYPS DIAVWESNG QPENNYKTPP PVLDSGDSFF LYSKLTVDKS 420
RWQQGNVFSQ SVMHEALHNH YTQKLSLSLP GKAPASSSTK KTQLQLEHLL LALQMILNGI 480
NNYKPKLITE MLTFKFYMPK KATELKHLCQ LEEELKPLEE VLNLAQSKNF HLRPRDLISN 540
INVIVLELKG SETTFMCEYA DETATIVEFL NRWITFAQSI ISTLT 585

-continued

SEQ ID NO: 472 moltype = AA length = 582
FEATURE Location/Qualifiers
source 1..582
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 472

| | | | | | | | | | | | | |
|--------|-------|--------|--------|--------|--------|--------|-------|--------|-------|--------|-------|-----|
| EVQLES | GGG | LVQPGG | SLRL | SCAASG | FTFK | DYCMTW | VRQA | PGKGLE | WVSA | IVYSGG | STYY | 60 |
| ADSVK | GRFTI | SRDNSK | NKNTLY | LQMN | NLRAED | TAVYYC | AKYK | RASYFY | DAMD | VWGQGT | TVTV | 120 |
| SSAST | KGPSV | FPLAPC | SRST | SESTA | ALGCL | VKDYFP | PEPVT | VSWNSG | GALTS | GVHTFP | PAVLQ | 180 |
| SSGLY | SLSSV | VTVPSS | SLGT | KTYTC | NVDHK | PSNTK | VDKRV | ESKYGP | PCPP | CPAPEF | EGGP | 240 |
| SVFLP | PKPK | DTLMIS | RTP | VTCVV | VDSQ | EDPEV | QFNWY | VDGVE | VHNAK | TKPREE | QFNS | 300 |
| TYRVV | SVLTV | LHQD | WLNKE | YKCKV | SNKGL | PSSIEK | TISK | AKGQPR | EPQV | YTLPPS | QEEM | 360 |
| TKNQV | SLTCL | VKGFYP | SDIA | VEWES | NGQPE | NNYKT | TPPVL | DSGGS | FFLYS | RLTVDK | SRWQ | 420 |
| EGNVF | SCSVM | HEALHN | HYTQ | KSLSL | SLGKA | PASSST | KKTKQ | LQLEH | LLAL | QMILNG | INNY | 480 |
| KNPKL | EMLT | FKFYMP | KKAT | ELKHL | QCLEE | ELKPLE | EVLN | LAQSK | NFHLR | PRDLIS | NINV | 540 |
| IVLEL | KGSET | TFMCEY | ADET | ATIVEF | LNLRW | ITFAQS | IIIST | LT | | | | 582 |

SEQ ID NO: 473 moltype = AA length = 582
FEATURE Location/Qualifiers
source 1..582
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 473

| | | | | | | | | | | | | |
|--------|-------|--------|--------|--------|--------|--------|-------|--------|-------|--------|-------|-----|
| EVQLES | GGG | LVQPGG | SLRL | SCAASG | FTFK | DYCMTW | VRQA | PGKGLE | WVSA | IVYSGG | STYY | 60 |
| ADSVK | GRFTI | SRDNSK | NKNTLY | LQMN | NLRAED | TAVYYC | AKYK | RASYFY | DAMD | VWGQGT | TVTV | 120 |
| SSAST | KGPSV | FPLAPC | SRST | SESTA | ALGCL | VKDYFP | PEPVT | VSWNSG | GALTS | GVHTFP | PAVLQ | 180 |
| SSGLY | SLSSV | VTVPSS | SLGT | KTYTC | NVDHK | PSNTK | VDKRV | ESKYGP | PCPP | CPAPEF | PAGAP | 240 |
| SVFLP | PKPK | DTLMIS | RTP | VTCVV | VDSQ | EDPEV | QFNWY | VDGVE | VHNAK | TKPREE | QFNS | 300 |
| TYRVV | SVLTV | LHQD | WLNKE | YKCKV | SNKGL | PSSIEK | TISK | AKGQPR | EPQV | YTLPPS | QEEM | 360 |
| TKNQV | SLTCL | VKGFYP | SDIA | VEWES | NGQPE | NNYKT | TPPVL | DSGGS | FFLYS | RLTVDK | SRWQ | 420 |
| EGNVF | SCSVM | HEALHN | HYTQ | KSLSL | SLGKA | PASSST | KKTKQ | LQLEH | LLAL | QMILNG | INNY | 480 |
| KNPKL | EMLT | FKFYMP | KKAT | ELKHL | QCLEE | ELKPLE | EVLN | LAQSK | NFHLR | PRDLIS | NINV | 540 |
| IVLEL | KGSET | TFMCEY | ADET | ATIVEF | LNLRW | ITFAQS | IIIST | LT | | | | 582 |

SEQ ID NO: 474 moltype = AA length = 585
FEATURE Location/Qualifiers
source 1..585
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 474

| | | | | | | | | | | | | |
|--------|--------|--------|--------|--------|--------|--------|-------|--------|-------|--------|-------|-----|
| EVQLES | GGG | LVQPGG | SLRL | SCAASG | FTFK | DYCMTW | VRQA | PGKGLE | WVSA | IVYSGG | STYY | 60 |
| ADSVK | GRFTI | SRDNSK | NKNTLY | LQMN | NLRAED | TAVYYC | AKYK | RASYFY | DAMD | VWGQGT | TVTV | 120 |
| SSAST | KGPSV | FPLAPC | SKST | SGGTA | ALGCL | VKDYFP | PEPVT | VSWNSG | GALTS | GVHTFP | PAVLQ | 180 |
| SSGLY | SLSSV | VTVPSS | SLGT | QTYIC | NVNHK | PSNTK | VDKRV | EPKSCD | KTHT | CPPCPA | PELA | 240 |
| GAPSV | FLPPP | KPKDTL | MISR | TPEVT | CVVD | VSHED | PEVKF | NWYVD | GVVH | NAKTKP | REEQ | 300 |
| YNSTY | RVVSV | LTVLHQ | DWLN | GKEYK | CKVSN | KALPA | PIEKT | ISKAKG | QPRE | PQVYTL | PPSR | 360 |
| DELTK | NQVSL | TCLVKG | FYPS | DIAVE | WESNG | QPENNY | KTP | PVLDS | DGFF | LYSKLT | VDKS | 420 |
| RWQGN | VFSC | SVMHEA | LHNH | YTQKS | LSP | GKAPAS | SSTK | KTQLQ | LEHLL | LDLQMI | LNGI | 480 |
| NNYKN | PKLTE | MLTFK | FYMPK | KATEL | KHLQC | LEEEL | KPLEE | VLNLA | QSKNF | HLRPRD | LISN | 540 |
| INVK | VLELKG | SETTFM | CEYA | DETATI | VEFL | NRWIT | FAQSI | ISTLT | | | | 585 |

SEQ ID NO: 475 moltype = AA length = 582
FEATURE Location/Qualifiers
source 1..582
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 475

| | | | | | | | | | | | | |
|--------|-------|--------|--------|--------|--------|--------|-------|--------|-------|--------|-------|-----|
| EVQLES | GGG | LVQPGG | SLRL | SCAASG | FTFK | DYCMTW | VRQA | PGKGLE | WVSA | IVYSGG | STYY | 60 |
| ADSVK | GRFTI | SRDNSK | NKNTLY | LQMN | NLRAED | TAVYYC | AKYK | RASYFY | DAMD | VWGQGT | TVTV | 120 |
| SSAST | KGPSV | FPLAPC | SRST | SESTA | ALGCL | VKDYFP | PEPVT | VSWNSG | GALTS | GVHTFP | PAVLQ | 180 |
| SSGLY | SLSSV | VTVPSS | SLGT | KTYTC | NVDHK | PSNTK | VDKRV | ESKYGP | PCPP | CPAPEF | EGGP | 240 |
| SVFLP | PKPK | DTLMIS | RTP | VTCVV | VDSQ | EDPEV | QFNWY | VDGVE | VHNAK | TKPREE | QFNS | 300 |
| TYRVV | SVLTV | LHQD | WLNKE | YKCKV | SNKGL | PSSIEK | TISK | AKGQPR | EPQV | YTLPPS | QEEM | 360 |
| TKNQV | SLTCL | VKGFYP | SDIA | VEWES | NGQPE | NNYKT | TPPVL | DSGGS | FFLYS | RLTVDK | SRWQ | 420 |
| EGNVF | SCSVM | HEALHN | HYTQ | KSLSL | SLGKA | PASSST | KKTKQ | LQLEH | LLDL | QMILNG | INNY | 480 |
| KNPKL | EMLT | FKFYMP | KKAT | ELKHL | QCLEE | ELKPLE | EVLN | LAQSK | NFHLR | PRDLIS | NINV | 540 |
| KVLEL | KGSET | TFMCEY | ADET | ATIVEF | LNLRW | ITFAQS | IIIST | LT | | | | 582 |

SEQ ID NO: 476 moltype = AA length = 582
FEATURE Location/Qualifiers
source 1..582
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 476

| | | | | | | | | | | | | |
|--------|-------|--------|--------|--------|--------|--------|-------|--------|-------|--------|-------|-----|
| EVQLES | GGG | LVQPGG | SLRL | SCAASG | FTFK | DYCMTW | VRQA | PGKGLE | WVSA | IVYSGG | STYY | 60 |
| ADSVK | GRFTI | SRDNSK | NKNTLY | LQMN | NLRAED | TAVYYC | AKYK | RASYFY | DAMD | VWGQGT | TVTV | 120 |
| SSAST | KGPSV | FPLAPC | SRST | SESTA | ALGCL | VKDYFP | PEPVT | VSWNSG | GALTS | GVHTFP | PAVLQ | 180 |
| SSGLY | SLSSV | VTVPSS | SLGT | KTYTC | NVDHK | PSNTK | VDKRV | ESKYGP | PCPP | CPAPEF | PAGAP | 240 |

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| | | | | | | |
|------------|------------|------------|------------|------------|------------|-----|
| SVFLFPPKPK | DTLMISRTP | VTCVVVDVSQ | EDPEVQFNWY | VDGVEVHNAK | TKPREEQFNS | 300 |
| TYRVVSVLTV | LHQDWLNGKE | YKCKVSNKGL | PSSIEKTISK | AKGQPREPQV | YTLPPSQEEM | 360 |
| TKNQVSLTCL | VKGFYPSDIA | VEWESNGQPE | NNYKTPPVV | DSGGSFFLYS | RLTVDKSRWQ | 420 |
| EGNVFSCSVM | HEALHNHYTQ | KSLSLSLGKA | PASSSTKKTQ | LQLEHLLLDL | QMILNGINNY | 480 |
| KNPKLTEMLT | FKFYMPKKAT | ELKHLQCLEE | ELKPLEEVLN | LAQSKNFHLR | PRDLISININ | 540 |
| KVLELKGSET | TFMCEYADET | ATIVEFLNRW | ITFAQSIIST | LT | | 582 |

SEQ ID NO: 477 moltype = AA length = 585
 FEATURE Location/Qualifiers
 source 1..585
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 477

| | | | | | | | | | | | | | | |
|-------------|-----|------------|-------|----------|------------|-------|---------|------|------|---------|-----|-----|------|-----|
| EVQLLES | GGG | LVQ | PGG | SLRL | SCAASGFTFK | DYCM | TWRQA | PGK | GLEW | VSA | IVY | SGG | STYY | 60 |
| ADSVKGRFTI | SRD | NSKNTLY | LQMN | NLRAED | TAVYYCAKYT | RASY | FYDAMD | VWG | QGT | TVTV | | | | 120 |
| SSASTKGPSV | FPL | APCSRST | SESTA | ALGCL | VKDYFPEPVT | VSWN | SGALTS | GVHT | FP | PAVLQ | | | | 180 |
| SSGLYSLSSV | VTV | PSSSLGT | QTYI | CNVNKH | PSNTKVDKVV | EPK | SCDKTHT | CP | PC | PAPELA | | | | 240 |
| GAPSVFLFPP | KPK | DTLMISR | TPEV | TCVVVD | VSHEDPEVKF | NWY | VDGVEVH | NAK | TK | PREEQ | | | | 300 |
| YNSTRYRVVSV | LT | VLHQDWLN | GKEY | KCKVSN | KALPAPIEKT | ISK | AKGQPRE | PQ | Y | YTLPPSR | | | | 360 |
| DELTKNQVSL | TCL | VKGFYPS | DI | AVEWESNG | QPENNYKTTT | PVLD | SDGSFF | LY | SK | LTVDKS | | | | 420 |
| RWQQGNVFS | C | SVMHEALHNH | YTQ | KSLSLSP | GKAPASSSTK | KTQ | LQLEHLL | LDL | Q | MILNGI | | | | 480 |
| NNYKNPKLTE | ML | TFKYMPK | KATE | LKHLQC | LEELKPLEE | VLN | LAQSKNF | HLR | PR | KLISN | | | | 540 |
| INVIVLELKG | SET | TFMCEYA | DET | ATIVEFL | NRWITFAQSI | ISTLT | | | | | | | | 585 |

SEQ ID NO: 478 moltype = AA length = 582
 FEATURE Location/Qualifiers
 source 1..582
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 478

| | | | | | | | | | | | | | | |
|------------|------------|------------|------------|------------|------------|------|--------|------|------|---------|-----|-----|------|-----|
| EVQLLES | GGG | LVQ | PGG | SLRL | SCAASGFTFK | DYCM | TWRQA | PGK | GLEW | VSA | IVY | SGG | STYY | 60 |
| ADSVKGRFTI | SRD | NSKNTLY | LQMN | NLRAED | TAVYYCAKYT | RASY | FYDAMD | VWG | QGT | TVTV | | | | 120 |
| SSASTKGPSV | FPL | APCSRST | SESTA | ALGCL | VKDYFPEPVT | VSWN | SGALTS | GVHT | FP | PAVLQ | | | | 180 |
| SSGLYSLSSV | VTV | PSSSLGT | KTYT | CNVNKH | PSNTKVDKRV | ESKY | GPPCPP | CP | AP | PEFEGGP | | | | 240 |
| SVFLFPPKPK | DTLMISRTP | VTCVVVDVSQ | EDPEVQFNWY | VDGVEVHNAK | TKPREEQFNS | 300 | | | | | | | | |
| TYRVVSVLTV | LHQDWLNGKE | YKCKVSNKGL | PSSIEKTISK | AKGQPREPQV | YTLPPSQEEM | 360 | | | | | | | | |
| TKNQVSLTCL | VKGFYPSDIA | VEWESNGQPE | NNYKTPPVV | DSGGSFFLYS | RLTVDKSRWQ | 420 | | | | | | | | |
| EGNVFSCSVM | HEALHNHYTQ | KSLSLSLGKA | PASSSTKKTQ | LQLEHLLLDL | QMILNGINNY | 480 | | | | | | | | |
| KNPKLTEMLT | FKFYMPKKAT | ELKHLQCLEE | ELKPLEEVLN | LAQSKNFHLR | PRDLISININ | 540 | | | | | | | | |
| IVLELKGSET | TFMCEYADET | ATIVEFLNRW | ITFAQSIIST | LT | | 582 | | | | | | | | |

SEQ ID NO: 479 moltype = AA length = 582
 FEATURE Location/Qualifiers
 source 1..582
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 479

| | | | | | | | | | | | | | | |
|------------|------------|------------|------------|------------|------------|------|--------|------|------|---------|-----|-----|------|-----|
| EVQLLES | GGG | LVQ | PGG | SLRL | SCAASGFTFK | DYCM | TWRQA | PGK | GLEW | VSA | IVY | SGG | STYY | 60 |
| ADSVKGRFTI | SRD | NSKNTLY | LQMN | NLRAED | TAVYYCAKYT | RASY | FYDAMD | VWG | QGT | TVTV | | | | 120 |
| SSASTKGPSV | FPL | APCSRST | SESTA | ALGCL | VKDYFPEPVT | VSWN | SGALTS | GVHT | FP | PAVLQ | | | | 180 |
| SSGLYSLSSV | VTV | PSSSLGT | KTYT | CNVNKH | PSNTKVDKRV | ESKY | GPPCPP | CP | AP | PEFAGAP | | | | 240 |
| SVFLFPPKPK | DTLMISRTP | VTCVVVDVSQ | EDPEVQFNWY | VDGVEVHNAK | TKPREEQFNS | 300 | | | | | | | | |
| TYRVVSVLTV | LHQDWLNGKE | YKCKVSNKGL | PSSIEKTISK | AKGQPREPQV | YTLPPSQEEM | 360 | | | | | | | | |
| TKNQVSLTCL | VKGFYPSDIA | VEWESNGQPE | NNYKTPPVV | DSGGSFFLYS | RLTVDKSRWQ | 420 | | | | | | | | |
| EGNVFSCSVM | HEALHNHYTQ | KSLSLSLGKA | PASSSTKKTQ | LQLEHLLLDL | QMILNGINNY | 480 | | | | | | | | |
| KNPKLTEMLT | FKFYMPKKAT | ELKHLQCLEE | ELKPLEEVLN | LAQSKNFHLR | PRDLISININ | 540 | | | | | | | | |
| IVLELKGSET | TFMCEYADET | ATIVEFLNRW | ITFAQSIIST | LT | | 582 | | | | | | | | |

SEQ ID NO: 480 moltype = AA length = 577
 FEATURE Location/Qualifiers
 source 1..577
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 480

| | | | | | | | | | | | | | | |
|-------------|-----|------------|------|----------|------------|-------|---------|------|------|-------|-----|------|------|-----|
| EVQLVES | GGG | LVQ | PGR | SLKL | SCAVSGFTFS | DYAMA | WVRQA | PKK | GLEW | VAT | ISY | DGSR | TYY | 60 |
| RDSVKGRFTI | SRD | NAK | TLY | LQMD | SLRSED | TATYY | CARHG | SGY | FDY | WGQ | VM | VT | VS | 120 |
| KGPSVFPPLAP | CSR | STSSSTA | ALG | LVKDYF | PEPVTVSWNS | GAL | TSGVHTF | PAV | LQ | SSGLY | | | | 180 |
| SLSSVVTVPS | SSL | GTKKTYT | C | NVD | HKPSNTK | VDKR | VESKYG | PP | CP | PAPE | FL | GG | P | 240 |
| PKPKDTLMI | SRT | PEVTCVV | VDV | SQEDPEV | QFNWYVDGVE | VHNA | KTKPRE | E | Q | FN | STY | RVV | | 300 |
| SVLTVLHQDW | LNG | KEYKCKV | SNK | GLPSSIE | KTISAKAGQP | REP | QVYTLPP | S | Q | E | M | T | KNQV | 360 |
| SLTCLVKG | FY | PSDIAVEWES | NGQ | PENNYKT | TPPVLDSDGS | FFLY | SRLTV | D | K | S | R | Q | E | 420 |
| SCSVMHEALH | NHY | TQKSLSL | SLG | KAPTSS | TKKTQLQLEH | LLLDL | Q | MILN | G | I | N | Y | K | 480 |
| TRMLTFKPYM | PKK | ATELKH | L | QLEELKPL | EVLNLAQSK | NFHL | RPRDLI | S | N | I | N | I | V | 540 |
| KGSETTFMCE | YAD | ETATIVE | FLNR | WITFCQ | SIISTLT | | | | | | | | | 577 |

SEQ ID NO: 481 moltype = AA length = 583
 FEATURE Location/Qualifiers
 source 1..583
 mol_type = protein

-continued

organism = Synthetic construct

SEQUENCE: 481

| | | | | | | |
|-------------|------------|-------------|------------|------------|------------|-----|
| EVQLVESGGG | LVQPGRSLKL | SCAVSGFTFS | DYAMAWRQA | PKKGLEWVAT | ISYDGSRTYY | 60 |
| RDSVKGRFTI | SRDNAKITLY | LQMDSLRSED | TATYYCARHG | SGYFDYWGG | VMVTVSSAST | 120 |
| KGPSVFPPLAP | CSRSTSESTA | ALGCLVKDYF | PEPVTVSWNS | GALTSGVHTF | PAVLQSSGLY | 180 |
| SLSSVVTVPS | SSLGTKTYTC | NVDHKPSNTK | VDKRVESKYG | PPCPPCPAPE | FLGGPSVFLF | 240 |
| PPKPKDTLMI | SRTPEVTCVV | VDVSDQEDPEV | QFNWYVDGVE | VHNAKTKPRE | EQFNSTYRVV | 300 |
| SVLTVLHQDW | LNGKEYKCKV | SNKGLPSSIE | KTISKAKGQP | REPQVYTLPP | SQEEMTKNQV | 360 |
| SLTCLVKGFY | PSDIAVEWES | NGQPENNYKT | TPPVLDSDGS | FFLYSRLTVD | KSRWQEGNVF | 420 |
| SCSVMHEALH | NHYTQKLSL | SLGKSGGGGS | APTSSSTKKT | QLQLEHLLLD | LQMILNGINN | 480 |
| YKNPKLTRML | TFKFYMPKKA | TELKHLQCLE | EELKPLEEVL | NLAQSKNFHL | RPRDLISNIN | 540 |
| VIVLELKGSE | TFMCEYADE | TATIVEFLNR | WITFCQSIIS | TLT | | 583 |

SEQ ID NO: 482 moltype = AA length = 443

FEATURE Location/Qualifiers

source 1..443

 mol_type = protein

 organism = Synthetic construct

SEQUENCE: 482

| | | | | | | |
|-------------|------------|-------------|------------|------------|------------|-----|
| EVQLVESGGG | LVQPGRSLKL | SCAVSGFTFS | DYAMAWRQA | PKKGLEWVAT | ISYDGSRTYY | 60 |
| RDSVKGRFTI | SRDNAKITLY | LQMDSLRSED | TATYYCARHG | SGYFDYWGG | VMVTVSSAST | 120 |
| KGPSVFPPLAP | CSRSTSESTA | ALGCLVKDYF | PEPVTVSWNS | GALTSGVHTF | PAVLQSSGLY | 180 |
| SLSSVVTVPS | SSLGTKTYTC | NVDHKPSNTK | VDKRVESKYG | PPCPPCPAPE | FLGGPSVFLF | 240 |
| PPKPKDTLMI | SRTPEVTCVV | VDVSDQEDPEV | QFNWYVDGVE | VHNAKTKPRE | EQFNSTYRVV | 300 |
| SVLTVLHQDW | LNGKEYKCKV | SNKGLPSSIE | KTISKAKGQP | REPQVYTLPP | SQEEMTKNQV | 360 |
| SLTCLVKGFY | PSDIAVEWES | NGQPENNYKT | TPPVLDSDGS | FFLYSRLTVD | KSRWQEGNVF | 420 |
| SCSVMHEALH | NHYTQKLSL | SLG | | | | 443 |

SEQ ID NO: 483 moltype = AA length = 346

FEATURE Location/Qualifiers

source 1..346

 mol_type = protein

 organism = Synthetic construct

SEQUENCE: 483

| | | | | | | |
|------------|------------|------------|------------|------------|------------|-----|
| DTVLTQSPAL | AVSPGERVTI | SCRASESVRT | GVHWYQQKPG | QQPKLLIYGA | SNLESGVPAR | 60 |
| FSGSGSGTDF | TLTIDPVEAD | DTATYFCQQS | WNDPPTFGSG | TKLEIKRTVA | APSVFIFPPS | 120 |
| DEQLKSGTAS | VVCLLNNFYP | REAKVQWKVD | NALQSGNSQE | SVTEQDSKDS | TYSLSSTLTL | 180 |
| SKADYEKHKV | YACEVTHQGL | SSPVTKSPNR | GECAPTSST | KKTQLQLEHL | LLDLQMLNG | 240 |
| INNYKNPKLT | RMLTFKPYMP | KKATELKHQ | CLEELKPLE | EVLNLAQSKN | FHLRPRDLIS | 300 |
| NINIVLELK | GSETTFMCEY | ADETATIVEF | LNRWITFCQS | IISTLT | | 346 |

SEQ ID NO: 484 moltype = AA length = 352

FEATURE Location/Qualifiers

source 1..352

 mol_type = protein

 organism = Synthetic construct

SEQUENCE: 484

| | | | | | | |
|------------|------------|------------|------------|------------|------------|-----|
| DTVLTQSPAL | AVSPGERVTI | SCRASESVRT | GVHWYQQKPG | QQPKLLIYGA | SNLESGVPAR | 60 |
| FSGSGSGTDF | TLTIDPVEAD | DTATYFCQQS | WNDPPTFGSG | TKLEIKRTVA | APSVFIFPPS | 120 |
| DEQLKSGTAS | VVCLLNNFYP | REAKVQWKVD | NALQSGNSQE | SVTEQDSKDS | TYSLSSTLTL | 180 |
| SKADYEKHKV | YACEVTHQGL | SSPVTKSPNR | GECSGGGSA | PTSSSTKKTQ | LQLEHLLLDL | 240 |
| QMILNGINNY | KNPKLTRMLT | KFKYMPKAT | ELKHLQCLEE | ELKPLEEVLN | LAQSKNFHLR | 300 |
| PRDLISINIV | IVLELKGSET | TFMCEYADET | ATIVEFLNRW | ITFCQSIIST | LT | 352 |

SEQ ID NO: 485 moltype = AA length = 583

FEATURE Location/Qualifiers

source 1..583

 mol_type = protein

 organism = Synthetic construct

SEQUENCE: 485

| | | | | | | |
|-------------|------------|-------------|------------|------------|------------|-----|
| EVQLVESGGG | LVQPGRSLKL | SCAVSGFTFS | DYAMAWRQA | PKKGLEWVAT | ISYDGSRTYY | 60 |
| RDSVKGRFTI | SRDNAKITLY | LQMDSLRSED | TATYYCARHG | SGYFDYWGG | VMVTVSSAST | 120 |
| KGPSVFPPLAP | CSRSTSESTA | ALGCLVKDYF | PEPVTVSWNS | GALTSGVHTF | PAVLQSSGLY | 180 |
| SLSSVVTVPS | SSLGTKTYTC | NVDHKPSNTK | VDKRVESKYG | PPCPPCPAPE | FLGGPSVFLF | 240 |
| PPKPKDTLMI | SRTPEVTCVV | VDVSDQEDPEV | QFNWYVDGVE | VHNAKTKPRE | EQFNSTYRVV | 300 |
| SVLTVLHQDW | LNGKEYKCKV | SNKGLPSSIE | KTISKAKGQP | REPQVYTLPP | SQEEMTKNQV | 360 |
| SLTCLVKGFY | PSDIAVEWES | NGQPENNYKT | TPPVLDSDGS | FFLYSRLTVD | KSRWQEGNVF | 420 |
| SCSVMHEALH | NHYTQKLSL | SLGKSGGGGS | APTSSSTKKT | QLQLEHLLLY | LQMILNGINN | 480 |
| YKNPKLTRML | TFKFYMPKKA | TELKHLQCLE | EELKPLEEVL | NLAQSKNFHL | RPRDLISNIN | 540 |
| VIVLELKGSE | TFMCEYADE | TATIVEFLNR | WITFCQSIIS | TLT | | 583 |

SEQ ID NO: 486 moltype = AA length = 577

FEATURE Location/Qualifiers

source 1..577

 mol_type = protein

 organism = Synthetic construct

SEQUENCE: 486

| | | | | | | |
|------------|------------|------------|------------|------------|------------|-----|
| EVQLVESGGG | LVQPGRSLKL | SCAVSGFTFS | DYAMAWRQA | PKKGLEWVAT | ISYDGSRTYY | 60 |
| RDSVKGRFTI | SRDNAKITLY | LQMDSLRSED | TATYYCARHG | SGYFDYWGG | VMVTVSSAST | 120 |

-continued

| | | | | | | |
|------------|-------------|-------------|------------|------------|-------------|-----|
| KGPSVFPLAP | CSRSTSESTA | ALGCLVKDYF | PEPVTVSWNS | GALTSQVHTF | PAVLQSSGLY | 180 |
| SLSSVVTVPS | SSLGKTYTC | NVDHKPSNTK | VDKRVESKYG | PPCPPCPAPE | FLGGPSVFLF | 240 |
| PPKPKDTLMI | SRTPEVTCV | VDVSDQEDPEV | QFNWYVDGVE | VHNAKTKPRE | EQFNSTYRVV | 300 |
| SVLTVLHQDW | LNGKEYKCKV | SNKGLPSSIE | KTISKAKGQP | REPQVYTLPP | SQEEMTKNQV | 360 |
| SLTCLVKGFY | PSDIAVEWES | NGQPENNYKT | TPPVLDSDGS | FFLYSRLTVD | KSRWQEGNVF | 420 |
| SCSVMHEALH | NHYTQKLSLSL | SLGKAPTSSS | TKKTQLQLEH | LLLYLQMLLN | GINNYKNPKL | 480 |
| TRMLTFKPYM | PKKATELKH | QCLEEBLKPL | EEVLNLAQSK | NFHLRPRDLI | SNINIVIVLEL | 540 |
| KGSETTFMCE | YADETATIVE | FLNRWITFCQ | SIISTLT | | | 577 |

SEQ ID NO: 487 moltype = AA length = 580
FEATURE Location/Qualifiers
source 1..580
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 487

| | | | | | | |
|------------|-------------|-------------|------------|------------|-------------|-----|
| EVQLVESGGG | LVQPGRSLKL | SCAVSGFTFS | DYAMAWVRQA | PKKGLEWVAT | ISYDGSRTYY | 60 |
| RDSVKGRFTI | SRDNAKITLY | LQMDLSRSED | TATYYCARHG | SGYFDYWGQG | VMVTVSSAST | 120 |
| KGPSVFPLAP | CSRSTSESTA | ALGCLVKDYF | PEPVTVSWNS | GALTSQVHTF | PAVLQSSGLY | 180 |
| SLSSVVTVPS | SSLGKTYTC | NVDHKPSNTK | VDKRVESKYG | PPCPPCPAPE | FLGGPSVFLF | 240 |
| PPKPKDTLMI | SRTPEVTCV | VDVSDQEDPEV | QFNWYVDGVE | VHNAKTKPRE | EQFNSTYRVV | 300 |
| SVLTVLHQDW | LNGKEYKCKV | SNKGLPSSIE | KTISKAKGQP | REPQVYTLPP | SQEEMTKNQV | 360 |
| SLTCLVKGFY | PSDIAVEWES | NGQPENNYKT | TPPVLDSDGS | FFLYSRLTVD | KSRWQEGNVF | 420 |
| SCSVMHEALH | NHYTQKLSLSL | SLGKAPTSSS | TKKTQLQLEH | LLLYLQMLLN | GINNYKNPKL | 480 |
| TRMLTFKPYM | PKKATELKH | QCLEEBLKPL | EEVLNLAQSK | NFHLRPRDLI | SNINIVIVLEL | 540 |
| KGSETTFMCE | YADETATIVE | FLNRWITFCQ | SIISTLT | | | 577 |

SEQ ID NO: 488 moltype = AA length = 583
FEATURE Location/Qualifiers
source 1..583
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 488

| | | | | | | |
|------------|-------------|-------------|------------|------------|------------|-----|
| EVQLVESGGG | LVQPGRSLKL | SCAVSGFTFS | DYAMAWVRQA | PKKGLEWVAT | ISYDGSRTYY | 60 |
| RDSVKGRFTI | SRDNAKITLY | LQMDLSRSED | TATYYCARHG | SGYFDYWGQG | VMVTVSSAST | 120 |
| KGPSVFPLAP | CSRSTSESTA | ALGCLVKDYF | PEPVTVSWNS | GALTSQVHTF | PAVLQSSGLY | 180 |
| SLSSVVTVPS | SSLGKTYTC | NVDHKPSNTK | VDKRVESKYG | PPCPPCPAPE | FLGGPSVFLF | 240 |
| PPKPKDTLMI | SRTPEVTCV | VDVSDQEDPEV | QFNWYVDGVE | VHNAKTKPRE | EQFNSTYRVV | 300 |
| SVLTVLHQDW | LNGKEYKCKV | SNKGLPSSIE | KTISKAKGQP | REPQVYTLPP | SQEEMTKNQV | 360 |
| SLTCLVKGFY | PSDIAVEWES | NGQPENNYKT | TPPVLDSDGS | FFLYSRLTVD | KSRWQEGNVF | 420 |
| SCSVMHEALH | NHYTQKLSLSL | SLGKSGGGGS | APTSSSTKKT | QLQLEHLLLA | LQMILNGINN | 480 |
| YKNPKLTPLM | TFKPYMPKKA | TELKHLQCLE | EELKPLEEVL | NLAQSKNFHL | RPRDLISNIN | 540 |
| VIVLELKGSE | TFMCEYADE | TATIVEFLNR | WITFCQSIIS | TLT | | 583 |

SEQ ID NO: 489 moltype = AA length = 583
FEATURE Location/Qualifiers
source 1..583
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 489

| | | | | | | |
|------------|-------------|-------------|------------|------------|------------|-----|
| EVQLVESGGG | LVQPGRSLKL | SCAVSGFTFS | DYAMAWVRQA | PKKGLEWVAT | ISYDGSRTYY | 60 |
| RDSVKGRFTI | SRDNAKITLY | LQMDLSRSED | TATYYCARHG | SGYFDYWGQG | VMVTVSSAST | 120 |
| KGPSVFPLAP | CSRSTSESTA | ALGCLVKDYF | PEPVTVSWNS | GALTSQVHTF | PAVLQSSGLY | 180 |
| SLSSVVTVPS | SSLGKTYTC | NVDHKPSNTK | VDKRVESKYG | PPCPPCPAPE | FLGGPSVFLF | 240 |
| PPKPKDTLMI | SRTPEVTCV | VDVSDQEDPEV | QFNWYVDGVE | VHNAKTKPRE | EQFNSTYRVV | 300 |
| SVLTVLHQDW | LNGKEYKCKV | SNKGLPSSIE | KTISKAKGQP | REPQVYTLPP | SQEEMTKNQV | 360 |
| SLTCLVKGFY | PSDIAVEWES | NGQPENNYKT | TPPVLDSDGS | FFLYSRLTVD | KSRWQEGNVF | 420 |
| SCSVMHEALH | NHYTQKLSLSL | SLGKSGGGGS | APTSSSTKKT | QLQLEHLLLA | LQMILNGINN | 480 |
| YKNPKLTSM | TFKPYMPKKA | TELKHLQCLE | EELKPLEEVL | NLAQSKNFHL | RPRDLISNIN | 540 |
| VIVLELKGSE | TFMCEYADE | TATIVEFLNR | WITFCQSIIS | TLT | | 583 |

SEQ ID NO: 490 moltype = AA length = 583
FEATURE Location/Qualifiers
source 1..583
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 490

| | | | | | | |
|------------|-------------|-------------|------------|------------|------------|-----|
| EVQLVESGGG | LVQPGRSLKL | SCAVSGFTFS | DYAMAWVRQA | PKKGLEWVAT | ISYDGSRTYY | 60 |
| RDSVKGRFTI | SRDNAKITLY | LQMDLSRSED | TATYYCARHG | SGYFDYWGQG | VMVTVSSAST | 120 |
| KGPSVFPLAP | CSRSTSESTA | ALGCLVKDYF | PEPVTVSWNS | GALTSQVHTF | PAVLQSSGLY | 180 |
| SLSSVVTVPS | SSLGKTYTC | NVDHKPSNTK | VDKRVESKYG | PPCPPCPAPE | FLGGPSVFLF | 240 |
| PPKPKDTLMI | SRTPEVTCV | VDVSDQEDPEV | QFNWYVDGVE | VHNAKTKPRE | EQFNSTYRVV | 300 |
| SVLTVLHQDW | LNGKEYKCKV | SNKGLPSSIE | KTISKAKGQP | REPQVYTLPP | SQEEMTKNQV | 360 |
| SLTCLVKGFY | PSDIAVEWES | NGQPENNYKT | TPPVLDSDGS | FFLYSRLTVD | KSRWQEGNVF | 420 |
| SCSVMHEALH | NHYTQKLSLSL | SLGKSGGGGS | APTSSSTKKT | QLQLEHLLLA | LQMILNGINN | 480 |
| YKNPKLTDM | TFKPYMPKKA | TELKHLQCLE | EELKPLEEVL | NLAQSKNFHL | RPRDLISNIN | 540 |
| VIVLELKGSE | TFMCEYADE | TATIVEFLNR | WITFCQSIIS | TLT | | 583 |

SEQ ID NO: 491 moltype = AA length = 583
FEATURE Location/Qualifiers

-continued

```

source                1..583
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 491
EVQLVESGGG LVQPGRSLKL SCAVSGFTFS DYAMAWVRQA PPKGLEWVAT ISYDGSRTYY 60
RDSVKGRFTI SRDNAKITLY LQMDSLRSED TATYYCARHG SGYFDYWGQG VMVTVSSAST 120
KGPSVFPLAP CSRSTSESTA ALGCLVKDYF PEPVTVSWNS GALTSGVHTF PAVLQSSGLY 180
SLSSVVTVPS SSLGTKTYTC NVDHKPSNTK VDKRVESKYG PPCPPCPAPE FLGGPSVFLF 240
PPKPKDTLMI SRTPEVTCVV VDVSQEDPEV QFNWYVDGVE VHNAKTKPRE EQFNSTYRVV 300
SVLTVLHQDW LNGKEYKCKV SNKGLPSSIE KTISKAKGQP REPQVYTLPP SQEEMTKNQV 360
SLTCLVKGFY PSDIAVEWES NGQPENNYKT TPPVLDSGDS FFLYSRLTVD KSRWQEGNVF 420
SCSVMHEALH NHYTQKSLSL SLGKSGGGGS APTSSSTKKT QLQLEHLLLA LQMILNGINN 480
YKNPKLTQML TFKFYMPKKA TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN 540
VIVLALKGSE TTFMCEYADE TATIVEFLNR WITFCQSIIS TLT 583

SEQ ID NO: 492        moltype = AA length = 583
FEATURE              Location/Qualifiers
source                1..583
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 492
EVQLVESGGG LVQPGRSLKL SCAVSGFTFS DYAMAWVRQA PPKGLEWVAT ISYDGSRTYY 60
RDSVKGRFTI SRDNAKITLY LQMDSLRSED TATYYCARHG SGYFDYWGQG VMVTVSSAST 120
KGPSVFPLAP CSRSTSESTA ALGCLVKDYF PEPVTVSWNS GALTSGVHTF PAVLQSSGLY 180
SLSSVVTVPS SSLGTKTYTC NVDHKPSNTK VDKRVESKYG PPCPPCPAPE FLGGPSVFLF 240
PPKPKDTLMI SRTPEVTCVV VDVSQEDPEV QFNWYVDGVE VHNAKTKPRE EQFNSTYRVV 300
SVLTVLHQDW LNGKEYKCKV SNKGLPSSIE KTISKAKGQP REPQVYTLPP SQEEMTKNQV 360
SLTCLVKGFY PSDIAVEWES NGQPENNYKT TPPVLDSGDS FFLYSRLTVD KSRWQEGNVF 420
SCSVMHEALH NHYTQKSLSL SLGKSGGGGS APTSSSTKKT QLQLEHLLLA LQMILNGINN 480
YKNPKLTRML THKFYMPKKA TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN 540
VIVLALKGSE TTFMCEYADE TATIVEFLNR WITFCQSIIS TLT 583

SEQ ID NO: 493        moltype = AA length = 583
FEATURE              Location/Qualifiers
source                1..583
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 493
EVQLVESGGG LVQPGRSLKL SCAVSGFTFS DYAMAWVRQA PPKGLEWVAT ISYDGSRTYY 60
RDSVKGRFTI SRDNAKITLY LQMDSLRSED TATYYCARHG SGYFDYWGQG VMVTVSSAST 120
KGPSVFPLAP CSRSTSESTA ALGCLVKDYF PEPVTVSWNS GALTSGVHTF PAVLQSSGLY 180
SLSSVVTVPS SSLGTKTYTC NVDHKPSNTK VDKRVESKYG PPCPPCPAPE FLGGPSVFLF 240
PPKPKDTLMI SRTPEVTCVV VDVSQEDPEV QFNWYVDGVE VHNAKTKPRE EQFNSTYRVV 300
SVLTVLHQDW LNGKEYKCKV SNKGLPSSIE KTISKAKGQP REPQVYTLPP SQEEMTKNQV 360
SLTCLVKGFY PSDIAVEWES NGQPENNYKT TPPVLDSGDS FFLYSRLTVD KSRWQEGNVF 420
SCSVMHEALH NHYTQKSLSL SLGKSGGGGS APTSSSTKKT QLQLEHLLLD LQMILNGINN 480
YKNPKLTDML TFKFYMPKKA TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN 540
VDVLELKGSE TTFMCEYADE TATIVEFLNR WITFCQSIIS TLT 583

SEQ ID NO: 494        moltype = AA length = 583
FEATURE              Location/Qualifiers
source                1..583
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 494
EVQLVESGGG LVQPGRSLKL SCAVSGFTFS DYAMAWVRQA PPKGLEWVAT ISYDGSRTYY 60
RDSVKGRFTI SRDNAKITLY LQMDSLRSED TATYYCARHG SGYFDYWGQG VMVTVSSAST 120
KGPSVFPLAP CSRSTSESTA ALGCLVKDYF PEPVTVSWNS GALTSGVHTF PAVLQSSGLY 180
SLSSVVTVPS SSLGTKTYTC NVDHKPSNTK VDKRVESKYG PPCPPCPAPE FLGGPSVFLF 240
PPKPKDTLMI SRTPEVTCVV VDVSQEDPEV QFNWYVDGVE VHNAKTKPRE EQFNSTYRVV 300
SVLTVLHQDW LNGKEYKCKV SNKGLPSSIE KTISKAKGQP REPQVYTLPP SQEEMTKNQV 360
SLTCLVKGFY PSDIAVEWES NGQPENNYKT TPPVLDSGDS FFLYSRLTVD KSRWQEGNVF 420
SCSVMHEALH NHYTQKSLSL SLGKSGGGGS APTSSSTKKT QLQLEHLLLD LQMILNGINN 480
YKNPKLTEML TFKFYMPKKA TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN 540
VDVLELKGSE TTFMCEYADE TATIVEFLNR WITFCQSIIS TLT 583

SEQ ID NO: 495        moltype = AA length = 583
FEATURE              Location/Qualifiers
source                1..583
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 495
EVQLVESGGG LVQPGRSLKL SCAVSGFTFS DYAMAWVRQA PPKGLEWVAT ISYDGSRTYY 60
RDSVKGRFTI SRDNAKITLY LQMDSLRSED TATYYCARHG SGYFDYWGQG VMVTVSSAST 120
KGPSVFPLAP CSRSTSESTA ALGCLVKDYF PEPVTVSWNS GALTSGVHTF PAVLQSSGLY 180
SLSSVVTVPS SSLGTKTYTC NVDHKPSNTK VDKRVESKYG PPCPPCPAPE FLGGPSVFLF 240
PPKPKDTLMI SRTPEVTCVV VDVSQEDPEV QFNWYVDGVE VHNAKTKPRE EQFNSTYRVV 300
SVLTVLHQDW LNGKEYKCKV SNKGLPSSIE KTISKAKGQP REPQVYTLPP SQEEMTKNQV 360
SLTCLVKGFY PSDIAVEWES NGQPENNYKT TPPVLDSGDS FFLYSRLTVD KSRWQEGNVF 420

```

-continued

```
SCSVMHEALH NHYTQKLSLSL SLGKSGGGGS APTSSSTKKT QLQLEHLLLD LQMILNGINN 480
YKNPKLTRML THKFYMPKKA TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN 540
VDVLELKGSE TTFMCEYADE TATIVEFLNR WITFCQSIIS TLT 583
```

```
SEQ ID NO: 496      moltype = AA length = 583
FEATURE            Location/Qualifiers
source             1..583
                  mol_type = protein
                  organism = Synthetic construct
```

```
SEQUENCE: 496
EVQLVESGGG LVQPGRSLKL SCAVSGFTFS DYAMAWVRQA PPKGLEWVAT ISYDGSRTYY 60
RDSVKGRFTI SRDNAKITLY LQMDSLRSED TATYYCARHG SGYFDYWGQG VMVTVSSAST 120
KGPSVFPLAP CSRSTSESTA ALGCLVKDYF PEPVTVSWNS GALTSGVHTF PAVLQSSGLY 180
SLSSVVTVPS SSLGTKTYTC NVDHKPSNTK VDKRVESKYG PPCPPCPAPE FLGGPSVFLF 240
PPKPKDTLMI SRTPEVTCVV VDVSQEDPEV QFNWYVDGVE VHNAKTKPRE EQFNSTYRVV 300
SVLTVLHQDW LNGKEYKCKV SNKGLPSSIE KTISKAKGQP REPQVYTLPP SQEEMTKNQV 360
SLTCLVKGFY PSDIAVEWES NGQPENNYKT TPPVLDSGGS FFLYSRLTVD KSRWQEGNVF 420
SCSVMHEALH NHYTQKLSLSL SLGKSGGGGS APTSSSTKKT QLQLEHLLLA LQMILNGINN 480
YKNPKLTEML TFKFYMPKKA TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN 540
VIVLELKGSE TTFMCEYADE TATIVEFLNR WITFCQSIIS TLT 583
```

```
SEQ ID NO: 497      moltype = AA length = 583
FEATURE            Location/Qualifiers
source             1..583
                  mol_type = protein
                  organism = Synthetic construct
```

```
SEQUENCE: 497
EVQLVESGGG LVQPGRSLKL SCAVSGFTFS DYAMAWVRQA PPKGLEWVAT ISYDGSRTYY 60
RDSVKGRFTI SRDNAKITLY LQMDSLRSED TATYYCARHG SGYFDYWGQG VMVTVSSAST 120
KGPSVFPLAP CSRSTSESTA ALGCLVKDYF PEPVTVSWNS GALTSGVHTF PAVLQSSGLY 180
SLSSVVTVPS SSLGTKTYTC NVDHKPSNTK VDKRVESKYG PPCPPCPAPE FLGGPSVFLF 240
PPKPKDTLMI SRTPEVTCVV VDVSQEDPEV QFNWYVDGVE VHNAKTKPRE EQFNSTYRVV 300
SVLTVLHQDW LNGKEYKCKV SNKGLPSSIE KTISKAKGQP REPQVYTLPP SQEEMTKNQV 360
SLTCLVKGFY PSDIAVEWES NGQPENNYKT TPPVLDSGGS FFLYSRLTVD KSRWQEGNVF 420
SCSVMHEALH NHYTQKLSLSL SLGKSGGGGS APASSSTKKT QLQLEHLLLA LQMILNGINN 480
YKNPKLTEML TFKFYMPKKA TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN 540
VIVLELKGSE TTFMCEYADE TATIVEFLNR WITFCQSIIS TLT 583
```

```
SEQ ID NO: 498      moltype = AA length = 583
FEATURE            Location/Qualifiers
source             1..583
                  mol_type = protein
                  organism = Synthetic construct
```

```
SEQUENCE: 498
EVQLVESGGG LVQPGRSLKL SCAVSGFTFS DYAMAWVRQA PPKGLEWVAT ISYDGSRTYY 60
RDSVKGRFTI SRDNAKITLY LQMDSLRSED TATYYCARHG SGYFDYWGQG VMVTVSSAST 120
KGPSVFPLAP CSRSTSESTA ALGCLVKDYF PEPVTVSWNS GALTSGVHTF PAVLQSSGLY 180
SLSSVVTVPS SSLGTKTYTC NVDHKPSNTK VDKRVESKYG PPCPPCPAPE FLGGPSVFLF 240
PPKPKDTLMI SRTPEVTCVV VDVSQEDPEV QFNWYVDGVE VHNAKTKPRE EQFNSTYRVV 300
SVLTVLHQDW LNGKEYKCKV SNKGLPSSIE KTISKAKGQP REPQVYTLPP SQEEMTKNQV 360
SLTCLVKGFY PSDIAVEWES NGQPENNYKT TPPVLDSGGS FFLYSRLTVD KSRWQEGNVF 420
SCSVMHEALH NHYTQKLSLSL SLGKSGGGGS APTSSSTKKT QLQLEHLLLA LQMILNGINN 480
YKNPKLTEML TFKFYMPKKA TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN 540
VIVLELKGSE TTFMCEYADE TATIVEFLNR WITFAQSIIS TLT 583
```

```
SEQ ID NO: 499      moltype = AA length = 583
FEATURE            Location/Qualifiers
source             1..583
                  mol_type = protein
                  organism = Synthetic construct
```

```
SEQUENCE: 499
EVQLVESGGG LVQPGRSLKL SCAVSGFTFS DYAMAWVRQA PPKGLEWVAT ISYDGSRTYY 60
RDSVKGRFTI SRDNAKITLY LQMDSLRSED TATYYCARHG SGYFDYWGQG VMVTVSSAST 120
KGPSVFPLAP CSRSTSESTA ALGCLVKDYF PEPVTVSWNS GALTSGVHTF PAVLQSSGLY 180
SLSSVVTVPS SSLGTKTYTC NVDHKPSNTK VDKRVESKYG PPCPPCPAPE FLGGPSVFLF 240
PPKPKDTLMI SRTPEVTCVV VDVSQEDPEV QFNWYVDGVE VHNAKTKPRE EQFNSTYRVV 300
SVLTVLHQDW LNGKEYKCKV SNKGLPSSIE KTISKAKGQP REPQVYTLPP SQEEMTKNQV 360
SLTCLVKGFY PSDIAVEWES NGQPENNYKT TPPVLDSGGS FFLYSRLTVD KSRWQEGNVF 420
SCSVMHEALH NHYTQKLSLSL SLGKSGGGGS APASSSTKKT QLQLEHLLLA LQMILNGINN 480
YKNPKLTEML TFKFYMPKKA TELKHLQCLE EELKPLEEVL NLAQSKNFHL RPRDLISNIN 540
VIVLELKGSE TTFMCEYADE TATIVEFLNR WITFAQSIIS TLT 583
```

```
SEQ ID NO: 500      moltype = AA length = 586
FEATURE            Location/Qualifiers
source             1..586
                  mol_type = protein
                  organism = Synthetic construct
```

```
SEQUENCE: 500
EVQLVESGGG LVQPGRSLKL SCAVSGFTFS DYAMAWVRQA PPKGLEWVAT ISYDGSRTYY 60
```

-continued

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RDSVKGRFTI SRDNAKITLY LQMDSLRSED TATYYCARHG SGYFDYWGQG VMVTVSSAST 120
KGPSVFPPLAP SSKSTSGGTA ALGCLVKDYF PEPVTVSWNS GALTSGVHTF PAVLQSSGLY 180
SLSSVVTVPS SSSLGTQTYIC NVNHKPSNTK VDKKVEPKSC DKHTHTCPPCP APELLGGPSV 240
FLFPPKPKDT LMISRTPEVT CVVVDVSHED PEVKFNWYVD GVEVHNAKTK PREEQYNSTY 300
RVVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK GQPREPQVYT LPPSRDELTK 360
NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTTPVLDS DGSFFLYSKL TVDKSRWQQG 420
NVFSCSVMHE ALHNHYTQKS LSLSPGKSGG GGSAPTSSST KKTQLQLEHL LALQMLING 480
INNYKNPKLT EMLTFKPYMP KKATELKHLO CLEEBLKPLE EVLNLAQSKN FHLRPRDLIS 540
NINIVLELKG SETTFMCEY ADETATIVEF LNRWITFCQS IISTLT 586

```

```

SEQ ID NO: 501      moltype = AA length = 586
FEATURE            Location/Qualifiers
source             1..586
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 501
EVQLVESGGG LVQPGRSLKL SCAVSGFTFS DYAMAWVRQA PPKGLEWVAT ISYDGSRTYY 60
RDSVKGRFTI SRDNAKITLY LQMDSLRSED TATYYCARHG SGYFDYWGQG VMVTVSSAST 120
KGPSVFPPLAP SSKSTSGGTA ALGCLVKDYF PEPVTVSWNS GALTSGVHTF PAVLQSSGLY 180
SLSSVVTVPS SSSLGTQTYIC NVNHKPSNTK VDKKVEPKSC DKHTHTCPPCP APELLGGPSV 240
FLFPPKPKDT LMISRTPEVT CVVVDVSHED PEVKFNWYVD GVEVHNAKTK PREEQYNSTY 300
RVVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK GQPREPQVYT LPPSRDELTK 360
NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTTPVLDS DGSFFLYSKL TVDKSRWQQG 420
NVFSCSVMHE ALHNHYTQKS LSLSPGKSGG GGSAPASSST KKTQLQLEHL LALQMLING 480
INNYKNPKLT EMLTFKPYMP KKATELKHLO CLEEBLKPLE EVLNLAQSKN FHLRPRDLIS 540
NINIVLELKG SETTFMCEY ADETATIVEF LNRWITFCQS IISTLT 586

```

```

SEQ ID NO: 502      moltype = AA length = 586
FEATURE            Location/Qualifiers
source             1..586
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 502
EVQLVESGGG LVQPGRSLKL SCAVSGFTFS DYAMAWVRQA PPKGLEWVAT ISYDGSRTYY 60
RDSVKGRFTI SRDNAKITLY LQMDSLRSED TATYYCARHG SGYFDYWGQG VMVTVSSAST 120
KGPSVFPPLAP SSKSTSGGTA ALGCLVKDYF PEPVTVSWNS GALTSGVHTF PAVLQSSGLY 180
SLSSVVTVPS SSSLGTQTYIC NVNHKPSNTK VDKKVEPKSC DKHTHTCPPCP APELLGGPSV 240
FLFPPKPKDT LMISRTPEVT CVVVDVSHED PEVKFNWYVD GVEVHNAKTK PREEQYNSTY 300
RVVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK GQPREPQVYT LPPSRDELTK 360
NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTTPVLDS DGSFFLYSKL TVDKSRWQQG 420
NVFSCSVMHE ALHNHYTQKS LSLSPGKSGG GGSAPTSSST KKTQLQLEHL LALQMLING 480
INNYKNPKLT EMLTFKPYMP KKATELKHLO CLEEBLKPLE EVLNLAQSKN FHLRPRDLIS 540
NINIVLELKG SETTFMCEY ADETATIVEF LNRWITFAQS IISTLT 586

```

```

SEQ ID NO: 503      moltype = AA length = 346
FEATURE            Location/Qualifiers
source             1..346
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 503
DTVLTQSPAL AVSPGERVTI SCRASESVRT GVHWYQQKPG QPKKLLIYGA SNLESGVPAR 60
FSGSGSGTDF TLTIDPVEAD DTATYFCQQS WNDPPTFGSG TKLEIKRTVA APSVFIFPPS 120
DEQLKSGTAS VVCLLNNFYP REAKVQWKVD NALQSGNSQE SVTEQDSKDS TYSLSSTLTL 180
SKADYEKHKV YACEVTHQGL SSPVTKSFNR GECAPTSST KKTQLQLEHL LALQMLING 240
INNYKNPKLT EMLTFKPYMP KKATELKHLO CLEEBLKPLE EVLNLAQSKN FHLRPRDLIS 300
NINIVLELKG SETTFMCEY ADETATIVEF LNRWITFCQS IISTLT 346

```

```

SEQ ID NO: 504      moltype = AA length = 352
FEATURE            Location/Qualifiers
source             1..352
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 504
DTVLTQSPAL AVSPGERVTI SCRASESVRT GVHWYQQKPG QPKKLLIYGA SNLESGVPAR 60
FSGSGSGTDF TLTIDPVEAD DTATYFCQQS WNDPPTFGSG TKLEIKRTVA APSVFIFPPS 120
DEQLKSGTAS VVCLLNNFYP REAKVQWKVD NALQSGNSQE SVTEQDSKDS TYSLSSTLTL 180
SKADYEKHKV YACEVTHQGL SSPVTKSFNR GECGSGGSSA PTSSTKKTQ LQLEHLLAL 240
QMILNGINNY KNPKLTEMLETFKPYMPKAT ELKHLQCLEE ELKPLEEVLN LAQSKNFHLR 300
PRDLISINIV IVLELKGSET TFMCEYADET ATIVEFLNRW ITFCQSIIST LT 352

```

```

SEQ ID NO: 505      moltype = AA length = 575
FEATURE            Location/Qualifiers
source             1..575
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 505
DVQLVESGGG VVRPAGESLRL SCTASGFTFS ISAMSWVRQA PGKGLEWVSA ISGTAYSTYY 60
ADSVRGRFTI SRDNSKNTLY LQMNLSRAED TAVYYCAKDN FFDYWGGLT VTVSSASTKG 120
PSVFPPLAPCS RSTSESTAAL GCLVKDYFPE PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL 180

```

-continued

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SSVVTVPSS LGTKTYTCNV DHKPSNTKVD KRVESKYGPP CPPCPAPEFL GGPSVFLFPP 240
KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWWYVDGVEVH NAKTKPREEQ FNSTYRVVSV 300
LTVLHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQPRE PQVYTLPPSQ EEMTKNQVSL 360
TCLVKGFYPS DIAVEWESNG QPENNYKTP PVLDSGDSFF LYSRLTVDKS RWQEGNVFSC 420
SVMHEALHNH YTQKSLSLSL GKAPTSSTK KTQLQLEHLL LALQMILNGI NNYKNPKLTE 480
MLTFKFYMPK KATELKHLC QLEELKPLEE VLNLAQSKNF HLRPRDLISN INVIVLELKG 540
SETTFMCEYA DETATIVEFL NRWITFCQSI ISTLT 575

```

```

SEQ ID NO: 506      moltype = AA length = 577
FEATURE            Location/Qualifiers
source             1..577
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 506
DVQLVESGGG VVRPGESLRL SCAASGFTFS TDAMGWVRQA PEGGLEWVSL ISGSGYSTYY 60
ADSVKGRFTI SRDNSKNTLY LQMNSLTAED TAVYYCAKNS LAFPDYWGGLG TLVTVSSAST 120
KGPSVFLPLAP CSRSTSESTA ALGCLVKDYF PEPVTVSWNS GALTSQVHTF PAVLQSSGLY 180
SLSSVVTVPS SSLGKTYTC NVDHKPSNTK VDKRVEKYG PPCPPAPE FLGGPSVFLF 240
PKPKDTLMI SRTPEVTCV VDSQEDPEV QFNWYVDGVE VHNNAKTKPRE EQFNSTYRVV 300
SVLTVLHQDW LNGKEYKCKV SNKGLPSSIE KTISKAKGQP REPQVYTLPP SQEEMTKNQV 360
SLTCLVKGFY PSDIAVEWES NGQPENNYKT TPPVLDSGDS FFLYSRLTVD KSRWQEGNVF 420
SCSVMHEALH NHYTQKSLSL SLGKAPTSST TKKTQLQLEH LLLALQMILN GINNYKNPKL 480
TEMLTFKFYM PKKATELKHLC QLEELKPLEE BEVLNLAQSK NFHLRPRDLI SNINVIVLEL 540
KGSETTFMCE YADETATIVE FLNRWITFCQ SIIISTLT 577

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```

SEQ ID NO: 507      moltype = AA length = 575
FEATURE            Location/Qualifiers
source             1..575
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 507
DVQLVESGGG VVRPGGSLRL SCAASGFTFS IYAMSWVRQA PEGGLEWVSH ISASGGSTYY 60
ADSVKGRFAI SRDNSKNTLY LQMNSLRAED TAVYYCTTNL GSDYWGGLGTL VTVSSASTKG 120
PSVFLPLAPCS RSTSESTAAL GCLVKDYFPE PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL 180
SSVVTVPSSS LGTKTYTCNV DHKPSNTKVD KRVESKYGPP CPPCPAPEFL GGPSVFLFPP 240
KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWWYVDGVEVH NAKTKPREEQ FNSTYRVVSV 300
LTVLHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQPRE PQVYTLPPSQ EEMTKNQVSL 360
TCLVKGFYPS DIAVEWESNG QPENNYKTP PVLDSGDSFF LYSRLTVDKS RWQEGNVFSC 420
SVMHEALHNH YTQKSLSLSL GKAPTSSTK KTQLQLEHLL LALQMILNGI NNYKNPKLTE 480
MLTFKFYMPK KATELKHLC QLEELKPLEE VLNLAQSKNF HLRPRDLISN INVIVLELKG 540
SETTFMCEYA DETATIVEFL NRWITFCQSI ISTLT 575

```

```

SEQ ID NO: 508      moltype = AA length = 575
FEATURE            Location/Qualifiers
source             1..575
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 508
DVQLVESGGG VVRPGGSLRL SCAASGFTFS IYAVSWVRQA PEGGLEWVSH ISASGGSTYY 60
ADSVKGRFAI SRDNSKNTLY LQMNSLRAED TAVYYCTTNL GSDYWGGLGTL VTVSSASTKG 120
PSVFLPLAPCS RSTSESTAAL GCLVKDYFPE PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL 180
SSVVTVPSSS LGTKTYTCNV DHKPSNTKVD KRVESKYGPP CPPCPAPEFL GGPSVFLFPP 240
KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWWYVDGVEVH NAKTKPREEQ FNSTYRVVSV 300
LTVLHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQPRE PQVYTLPPSQ EEMTKNQVSL 360
TCLVKGFYPS DIAVEWESNG QPENNYKTP PVLDSGDSFF LYSRLTVDKS RWQEGNVFSC 420
SVMHEALHNH YTQKSLSLSL GKAPTSSTK KTQLQLEHLL LALQMILNGI NNYKNPKLTE 480
MLTFKFYMPK KATELKHLC QLEELKPLEE VLNLAQSKNF HLRPRDLISN INVIVLELKG 540
SETTFMCEYA DETATIVEFL NRWITFCQSI ISTLT 575

```

```

SEQ ID NO: 509      moltype = AA length = 575
FEATURE            Location/Qualifiers
source             1..575
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 509
DVQLVESGGG LVQPGGSLRL SCAASGFTFD ISAMSWVRQA PGKGLEWVST ISGSAYSTYY 60
ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCAREI FSDYWGGLGTL VTVSSASTKG 120
PSVFLPLAPCS RSTSESTAAL GCLVKDYFPE PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL 180
SSVVTVPSSS LGTKTYTCNV DHKPSNTKVD KRVESKYGPP CPPCPAPEFL GGPSVFLFPP 240
KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWWYVDGVEVH NAKTKPREEQ FNSTYRVVSV 300
LTVLHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQPRE PQVYTLPPSQ EEMTKNQVSL 360
TCLVKGFYPS DIAVEWESNG QPENNYKTP PVLDSGDSFF LYSRLTVDKS RWQEGNVFSC 420
SVMHEALHNH YTQKSLSLSL GKAPTSSTK KTQLQLEHLL LALQMILNGI NNYKNPKLTR 480
MLTAKFYMPK KATELKHLC QLEELKPLEE VLNLAQSKNF HLRPRDLISN INVIVLELKG 540
SETTFMCEYA DETATIVEFL NRWITFCQSI ISTLT 575

```

```

SEQ ID NO: 510      moltype = AA length = 575
FEATURE            Location/Qualifiers
source             1..575

```

-continued

mol_type = protein
organism = Synthetic construct

SEQUENCE: 510
DVQLVESGGG LVQPGGSLRL SCAASGFTFD ISAMSWVRQA PGKGLEWVST ISGSAYSTYY 60
ADSVKGRFTI SRDNSKSTLY LQMNSLRAED TAVYYCAREI FSDYWGLGTL VTVSSASTKG 120
PSVFPPLAPCS RSTSESTAAL GCLVKDYFPE PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL 180
SSVTVPSST LGTKTYTCNV DHKPSNTKVD KRVESKYGPP CPPCPAPEFL GGPSVFLFPP 240
KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWYVDGVEVH NAKTKPREEQ FNSTYRVVSV 300
LTVLHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQPRE PQVYTLPPSQ EEMTKNQVSL 360
TCLVKGFYPS DIAVEWESNG QPENNYKTP PVLDSGDSFF LYSRLTVDKS RWQEGNVFSC 420
SVMHEALHNH YTQKSLSLSL GKAPTSSSTK KTQLQLEHLL LALQMLNGI NNYKNPKLTR 480
MLTSKFYMPK KATELKHLCQ LBEELKPLEE VLNLAQSKNF HLRPRDLISN INVIVLELKG 540
SETTFMCEYA DETATIVEFL NRWITFCQSI ISTLT 575

SEQ ID NO: 511 moltype = AA length = 575
FEATURE Location/Qualifiers
source 1..575
mol_type = protein
organism = Synthetic construct

SEQUENCE: 511
DVQLVESGGG LVQPGGSLRL SCAASGFTFD ISAMSWVRQA PGKGLEWVST ISGSAYSTYY 60
ADSVKGRFTI SRDNSKSTLY LQMNSLRAED TAVYYCAREI FSDYWGLGTL VTVSSASTKG 120
PSVFPPLAPCS RSTSESTAAL GCLVKDYFPE PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL 180
SSVTVPSST LGTKTYTCNV DHKPSNTKVD KRVESKYGPP CPPCPAPEFL GGPSVFLFPP 240
KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWYVDGVEVH NAKTKPREEQ FNSTYRVVSV 300
LTVLHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQPRE PQVYTLPPSQ EEMTKNQVSL 360
TCLVKGFYPS DIAVEWESNG QPENNYKTP PVLDSGDSFF LYSRLTVDKS RWQEGNVFSC 420
SVMHEALHNH YTQKSLSLSL GKAPTSSSTK KTQLQLEHLL LSLQMLNGI NNYKNPKLTE 480
MLTFKFYMPK KATELKHLCQ LBEELKPLEE VLNLAQSKNF HLRPRDLISN INVIVLELKG 540
SETTFMCEYA DETATIVEFL NRWITFCQSI ISTLT 575

SEQ ID NO: 512 moltype = AA length = 575
FEATURE Location/Qualifiers
source 1..575
mol_type = protein
organism = Synthetic construct

SEQUENCE: 512
DVQLVESGGG LVQPGGSLRL SCAASGFTFD ISAMSWVRQA PGKGLEWVST ISGSAYSTYY 60
ADSVKGRFTI SRDNSKSTLY LQMNSLRAED TAVYYCAREI FSDYWGLGTL VTVSSASTKG 120
PSVFPPLAPCS RSTSESTAAL GCLVKDYFPE PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL 180
SSVTVPSST LGTKTYTCNV DHKPSNTKVD KRVESKYGPP CPPCPAPEFL GGPSVFLFPP 240
KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWYVDGVEVH NAKTKPREEQ FNSTYRVVSV 300
LTVLHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQPRE PQVYTLPPSQ EEMTKNQVSL 360
TCLVKGFYPS DIAVEWESNG QPENNYKTP PVLDSGDSFF LYSRLTVDKS RWQEGNVFSC 420
SVMHEALHNH YTQKSLSLSL GKAPTSSSTK KTQLQLEHLL LDLQMLNGI NNYKNPKLTR 480
MLTAKFYMPK KATELKHLCQ LBEELKPLEE VLNLAQSKNF HLRPRDLISR INVIVLELKG 540
SETTFMCEYA DETATIVEFL NRWITFCQSI ISTLT 575

SEQ ID NO: 513 moltype = AA length = 575
FEATURE Location/Qualifiers
source 1..575
mol_type = protein
organism = Synthetic construct

SEQUENCE: 513
DVQLVESGGG LVQPGGSLRL SCAASGFTFD ISAMSWVRQA PGKGLEWVST ISGSAYSTYY 60
ADSVKGRFTI SRDNSKSTLY LQMNSLRAED TAVYYCAREI FSDYWGLGTL VTVSSASTKG 120
PSVFPPLAPCS RSTSESTAAL GCLVKDYFPE PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL 180
SSVTVPSST LGTKTYTCNV DHKPSNTKVD KRVESKYGPP CPPCPAPEFL GGPSVFLFPP 240
KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWYVDGVEVH NAKTKPREEQ FNSTYRVVSV 300
LTVLHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQPRE PQVYTLPPSQ EEMTKNQVSL 360
TCLVKGFYPS DIAVEWESNG QPENNYKTP PVLDSGDSFF LYSRLTVDKS RWQEGNVFSC 420
SVMHEALHNH YTQKSLSLSL GKAPTSSSTK KTQLQLEHLL LDLQMLNGI NNYKNPKLTR 480
MLTIKFYMPK KATELKHLCQ LBEELKPLEE VLNLAQSKNF HLRPRDLISN INVIVLELKG 540
SETTFMCEYA DETATIVEFL NRWITFCQSI ISTLT 575

SEQ ID NO: 514 moltype = AA length = 575
FEATURE Location/Qualifiers
source 1..575
mol_type = protein
organism = Synthetic construct

SEQUENCE: 514
DVQLVESGGG LVQPGGSLRL SCAASGFTFD ISAMSWVRQA PGKGLEWVST ISGSAYSTYY 60
ADSVKGRFTI SRDNSKSTLY LQMNSLRAED TAVYYCAREI FSDYWGLGTL VTVSSASTKG 120
PSVFPPLAPCS RSTSESTAAL GCLVKDYFPE PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL 180
SSVTVPSST LGTKTYTCNV DHKPSNTKVD KRVESKYGPP CPPCPAPEFL GGPSVFLFPP 240
KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWYVDGVEVH NAKTKPREEQ FNSTYRVVSV 300
LTVLHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQPRE PQVYTLPPSQ EEMTKNQVSL 360
TCLVKGFYPS DIAVEWESNG QPENNYKTP PVLDSGDSFF LYSRLTVDKS RWQEGNVFSC 420
SVMHEALHNH YTQKSLSLSL GKAPTSSSTK KTQLQLEHLL LDLQMLNGI NNYKNPKLTR 480

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MLTQKFYMPK KATELKHLC LEEELKPLEE VLNLAQSKNF HLRPRDLISN INVVDVLELKG 540
 SETTFMCEYA DETATIVEFL NRWITFCQSI ISTLT 575

SEQ ID NO: 515 moltype = AA length = 575
 FEATURE Location/Qualifiers
 source 1..575
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 515
 DVQLVESGGG LVQPGGSLRL SCAASGFTFD ISAMSWVRQA PGKGLEWVST ISGSAYSTYY 60
 ADSVKGRFTI SRDNSKSTLY LQMNSLRAED TAVYYCAREI FSDYWGGLGTL VTVSSASTKG 120
 PSVFPPLAPCS RSTSESTAAL GCLVKDYFPE PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL 180
 SSVVTVPSSS LGTKTYTCNV DHKPSNTKVD KRVESKYGPP CPPCPAPEFL GGPSVFLFPP 240
 KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NQYVDGVEVH NAKTKPREEQ FNSTYRVVSV 300
 LTVLHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQPRE PQVYTLPPSQ EEMTKNQVSL 360
 TCLVKGFPYS DIAVEWESNG QPENNYKTP PVLDSGDSFF LYSRLTVDKS RWQEGNVFSC 420
 SVMHEALHNH YTQKSLSLSL GKAPTSSTK KTQLQLEHLL LDLQMILNGI NNYKNPKLTR 480
 MLTQKFYMPK KATELKHLC LEEELKPLEE VLNLAQSKNF HLRPRDLISN INVVDVLELKG 540
 SETTFMCEYA DETATIVEFL NRWITFCQSI ISTLT 575

SEQ ID NO: 516 moltype = AA length = 575
 FEATURE Location/Qualifiers
 source 1..575
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 516
 DVQLVESGGG LVQPGGSLRL SCAASGFTFD ISAMSWVRQA PGKGLEWVST ISGSAYSTYY 60
 ADSVKGRFTI SRDNSKSTLY LQMNSLRAED TAVYYCAREI FSDYWGGLGTL VTVSSASTKG 120
 PSVFPPLAPCS RSTSESTAAL GCLVKDYFPE PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL 180
 SSVVTVPSSS LGTKTYTCNV DHKPSNTKVD KRVESKYGPP CPPCPAPEFL GGPSVFLFPP 240
 KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NQYVDGVEVH NAKTKPREEQ FNSTYRVVSV 300
 LTVLHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQPRE PQVYTLPPSQ EEMTKNQVSL 360
 TCLVKGFPYS DIAVEWESNG QPENNYKTP PVLDSGDSFF LYSRLTVDKS RWQEGNVFSC 420
 SVMHEALHNH YTQKSLSLSL GKAPTSSTK KTQLQLEHLL LDLQMILNGI NNYKNPKLTR 480
 MLTQKFYMPK KATELKHLC LEEELKPLEE VLNLAQSKNF HLRPRDLISN INVVDVLELKG 540
 SETTFMCEYA DETATIVEFL NRWITFCQSI ISTLT 575

SEQ ID NO: 517 moltype = AA length = 575
 FEATURE Location/Qualifiers
 source 1..575
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 517
 DVQLVESGGG LVQPGGSLRL SCAASGFTFD ISAMSWVRQA PGKGLEWVST ISGSAYSTYY 60
 ADSVKGRFTI SRDNSKSTLY LQMNSLRAED TAVYYCAREI FSDYWGGLGTL VTVSSASTKG 120
 PSVFPPLAPCS RSTSESTAAL GCLVKDYFPE PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL 180
 SSVVTVPSSS LGTKTYTCNV DHKPSNTKVD KRVESKYGPP CPPCPAPEFL GGPSVFLFPP 240
 KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NQYVDGVEVH NAKTKPREEQ FNSTYRVVSV 300
 LTVLHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQPRE PQVYTLPPSQ EEMTKNQVSL 360
 TCLVKGFPYS DIAVEWESNG QPENNYKTP PVLDSGDSFF LYSRLTVDKS RWQEGNVFSC 420
 SVMHEALHNH YTQKSLSLSL GKAPTSSTK KTQLQLEHLL LDLQMILNGI NNYKNPKLTE 480
 MLTQKFYMPK KATELKHLC LEEELKPLEE VLNLAQSKNF HLRPRDLISN INVVDVLELKG 540
 SETTFMCEYA DETATIVEFL NRWITFCQSI ISTLT 575

SEQ ID NO: 518 moltype = AA length = 575
 FEATURE Location/Qualifiers
 source 1..575
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 518
 DVQLVESGGG LVQPGGSLRL SCAASGFTFD ISAMSWVRQA PGKGLEWVST ISGSAYSTYY 60
 ADSVKGRFTI SRDNSKSTLY LQMNSLRAED TAVYYCAREI FSDYWGGLGTL VTVSSASTKG 120
 PSVFPPLAPCS RSTSESTAAL GCLVKDYFPE PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL 180
 SSVVTVPSSS LGTKTYTCNV DHKPSNTKVD KRVESKYGPP CPPCPAPEFL GGPSVFLFPP 240
 KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NQYVDGVEVH NAKTKPREEQ FNSTYRVVSV 300
 LTVLHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQPRE PQVYTLPPSQ EEMTKNQVSL 360
 TCLVKGFPYS DIAVEWESNG QPENNYKTP PVLDSGDSFF LYSRLTVDKS RWQEGNVFSC 420
 SVMHEALHNH YTQKSLSLSL GKAPTSSTK KTQLQLEHLL LDLQMILNGI NNYKNPKLTE 480
 MLTQKFYMPK KATELKHLC LEEELKPLEE VLNLAQSKNF HLRPRDLISN INVVDVLELKG 540
 SETTFMCEYA DETATIVEFL NRWITFCQSI ISTLT 575

SEQ ID NO: 519 moltype = AA length = 581
 FEATURE Location/Qualifiers
 source 1..581
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 519
 QVQLVQSGSE LKPKGASVKV SCKASGYSLY GTSMHWVRQA PGQGLEWGMGY ISPFTGRATY 60
 AQTGTRFVFL SLDTSVSTAY LQISSLKAED TAVYYCARDY DRYYYYAMDY WGQGTTVTVS 120

-continued

| | | | | | | |
|------------|-------------|------------|------------|------------|-------------|-----|
| SASTKGPSVF | PLAPCSRSTS | ESTAALGCLV | KDYFPEPVTV | SWNSGALTSG | VHTFPAVLQS | 180 |
| SGLYSLSSVV | TVPSSSLGTK | TYTCNVDPHK | SNTKVDKRVE | SKYGPCCPPC | PAPEFLGGPS | 240 |
| VFLFPPKPKD | TLMISRTPVEV | TCVVVDVSQE | DPEVQFNWYV | DGVEVHNAKT | KPREEQFNST | 300 |
| YRVVSVLTVL | HQDWLNGKEY | KCKVSNKGLP | SSIEKTISKA | KGQPREPQVY | TLPPSQEEMT | 360 |
| KNQVSLTCLV | KGFYPSDIAV | EWESNGQPEN | NYKTPPVLD | SDGSFFLYSR | LTVDKSRWQE | 420 |
| GNVFCSCVMH | EALHNHYTQK | SLSLSLGKAP | TSSSTKKTQL | QLEHLLALQ | MILNGINNYK | 480 |
| NPKLTEMLTF | KFYMPKKATE | LKHLQCLEEE | LKPLEEVLNL | AQSKNFHLRP | RDLISININVI | 540 |
| VLELKGSETT | FMCEYADETA | TIVEFLNRWI | TFCQSIISTL | T | | 581 |

SEQ ID NO: 520 moltype = AA length = 581
 FEATURE Location/Qualifiers
 source 1..581
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 520

| | | | | | | |
|------------|-------------|------------|------------|------------|-------------|-----|
| QVQLVQSGSE | LKKPGASVKV | SCKASGYSLY | GTSMHWRVQA | PGQGLEWNGY | ISPFTGRATY | 60 |
| AQGFTGRPVF | SLDTSVSTAY | LQISSLKAED | TAVYYCARDY | DYRYYYAMDY | WGQGTTVTVS | 120 |
| SASTKGPSVF | PLAPCSRSTS | ESTAALGCLV | KDYFPEPVTV | SWNSGALTSG | VHTFPAVLQS | 180 |
| SGLYSLSSVV | TVPSSSLGTK | TYTCNVDPHK | SNTKVDKRVE | SKYGPCCPPC | PAPEFEGGPS | 240 |
| VFLFPPKPKD | TLMISRTPVEV | TCVVVDVSQE | DPEVQFNWYV | DGVEVHNAKT | KPREEQFNST | 300 |
| YRVVSVLTVL | HQDWLNGKEY | KCKVSNKGLP | SSIEKTISKA | KGQPREPQVY | TLPPSQEEMT | 360 |
| KNQVSLTCLV | KGFYPSDIAV | EWESNGQPEN | NYKTPPVLD | SDGSFFLYSR | LTVDKSRWQE | 420 |
| GNVFCSCVMH | EALHNHYTQK | SLSLSLGKAP | ASSSTKKTQL | QLEHLLALQ | MILNGINNYK | 480 |
| NPKLTEMLTF | KFYMPKKATE | LKHLQCLEEE | LKPLEEVLNL | AQSKNFHLRP | RDLISININVI | 540 |
| VLELKGSETT | FMCEYADETA | TIVEFLNRWI | TFAQSIISTL | T | | 581 |

SEQ ID NO: 521 moltype = AA length = 581
 FEATURE Location/Qualifiers
 source 1..581
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 521

| | | | | | | |
|------------|-------------|------------|------------|------------|-------------|-----|
| QVQLVQSGSE | LKKPGASVKV | SCKASGYSLY | GTSMHWRVQA | PGQGLEWNGY | ISPFTGRATY | 60 |
| AQGFTGRPVF | SLDTSVSTAY | LQISSLKAED | TAVYYCARDY | DYRYYYAMDY | WGQGTTVTVS | 120 |
| SASTKGPSVF | PLAPCSRSTS | ESTAALGCLV | KDYFPEPVTV | SWNSGALTSG | VHTFPAVLQS | 180 |
| SGLYSLSSVV | TVPSSSLGTK | TYTCNVDPHK | SNTKVDKRVE | SKYGPCCPPC | PAPEFAGAPS | 240 |
| VFLFPPKPKD | TLMISRTPVEV | TCVVVDVSQE | DPEVQFNWYV | DGVEVHNAKT | KPREEQFNST | 300 |
| YRVVSVLTVL | HQDWLNGKEY | KCKVSNKGLP | SSIEKTISKA | KGQPREPQVY | TLPPSQEEMT | 360 |
| KNQVSLTCLV | KGFYPSDIAV | EWESNGQPEN | NYKTPPVLD | SDGSFFLYSR | LTVDKSRWQE | 420 |
| GNVFCSCVMH | EALHNHYTQK | SLSLSLGKAP | ASSSTKKTQL | QLEHLLALQ | MILNGINNYK | 480 |
| NPKLTEMLTF | KFYMPKKATE | LKHLQCLEEE | LKPLEEVLNL | AQSKNFHLRP | RDLISININVI | 540 |
| VLELKGSETT | FMCEYADETA | TIVEFLNRWI | TFAQSIISTL | T | | 581 |

SEQ ID NO: 522 moltype = AA length = 586
 FEATURE Location/Qualifiers
 source 1..586
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 522

| | | | | | | |
|------------|------------|-------------|------------|------------|------------|-----|
| EVQLVESGGG | LVQPGSRSLK | SCAVSGFTFS | DYAMAWVRQA | PKKGLEWVAT | ISYDGSRTYY | 60 |
| RDSVKGRFTI | SRDNAKITLY | LQMDLSRSED | TATYYCARHG | SGYFDYWGQG | VMVTVSSAST | 120 |
| KGPSVPLAPL | SSKSTSGGTA | ALGCLVKDYF | PEPVTVSWNS | GALTSGVHTF | PAVLQSSGLY | 180 |
| SLSSVTVTPS | SSLGTQTYIC | NVNHKPSNTK | VDKKVEPKSC | DKTHTCPPCP | APELAGAPSV | 240 |
| FLFPPKPKDT | LMISRTPVEV | CVVVDVSHED | PEVKFNWYVD | GVEVHNAKTK | PREEQYNSTY | 300 |
| RVVSVLTVLH | QDWLNGKEYK | CKVSNKALPA | PIEKTISKAK | GQPREPQVYT | LPPSRDELTK | 360 |
| NQVSLTCLVK | KGFYPSDIAV | WESNGQPENN | YKTPPVLDL | DGSFFLYSKL | TVDKSRWQQG | 420 |
| NVFCSCVMHE | ALHNHYTQKS | LSLSPGKSGG | GGAPASSTST | KKTQLQLEHL | LLALQMILNG | 480 |
| INNYKNPKLT | EMLTFKFYMP | KKATELKHLLQ | CLEELKPLE | EVLNLAQSKN | FHLRPRDLIS | 540 |
| NINIVLELKL | GSETTFMCEY | ADETATIVEF | LNRWITFAQS | IISTLT | | 586 |

SEQ ID NO: 523 moltype = AA length = 216
 FEATURE Location/Qualifiers
 source 1..216
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 523

| | | | | | | |
|------------|------------|------------|------------|-------------|------------|-----|
| EIVLTQSPGT | LSLSPGERAT | LSCRASQSIG | RSFLAWYQQK | PGQAPRLLIY | DASTRADIP | 60 |
| ARFSGSGSGT | DFTLTISLE | PEDFAVYCYQ | QYDWPPLSF | GGGTVKVEIKR | TVAAPSVFIF | 120 |
| PPSDEQLKSG | TASVVCLLMN | FYPREAKVQW | KVDNALQSGN | SQESVTEQDS | KDSTYLSST | 180 |
| LTLKADYEEK | HKVYACEVTH | QGLSSPVTKS | FNRGEC | | | 216 |

SEQ ID NO: 524 moltype = AA length = 582
 FEATURE Location/Qualifiers
 source 1..582
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 524

| | | | | | | |
|------------|------------|------------|------------|------------|------------|-----|
| EVQLLESGGG | LVQPGGSLRL | SCVSGGFNLK | DYCMTWVRQA | PGKLEWVSA | IVYSGGSTYY | 60 |
| ADSVKGRFTI | SRDNSKNTLY | LQMNLSRAED | TAVYYCAKYT | RGSYFYDAMD | VWGQGTTVTV | 120 |

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SSASTKGPSV FPLAPCSRST SESTAALGCL VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ 180
SSGLYSLSSV VTPSSSLGT KTYTCNVDPK PSNTKVDKRV ESKYGPPCPP CPAPEFLGGP 240
SVFLFPPKPK DTLMISRTP VTCVVVDVDSQ EDPEVQFNWY VDGVEVHNAK TKPREEQFNS 300
TYRVVSVLTV LHQDWLNGKE YKCKVSNKGL PSSIEKTISK AKGQPREPQV YTLPPSQEEM 360
TKNQVSLTCL VKGFYPSDIA VEWESNGQPE NNYKTTPPVL DSDGSFFLYS RLTVDKSRWQ 420
EGNVFSCSVM HEALHNHYTQ KSLSLSLGKA PTSSTKKTQ LQLEHLLAL QMILNGINNY 480
KNPKLTEMLT FKFYMPKKAT ELKHLQCLEE ELKPLEEVLN LAQSKNFHLR PRDLISINIV 540
IVLELKGSET TFMCEYADET ATIVEFLNRW ITFCQSIIST LT 582

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SEQ ID NO: 525          moltype = AA length = 216
FEATURE               Location/Qualifiers
source                1..216
                    mol_type = protein
                    organism = Synthetic construct

```

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SEQUENCE: 525
EIVLTQSPGT LSLSPGERAT LSCRASQSIG RSFLAWYQQK PGQAPRLLIY DASTRAADIP 60
DRFSGSGSGT DFTLTINRLE PEDFAVYCYQ QYYDWPPLTF GGGTKVEIKR TVAAPSVFIF 120
PPSDEQLKSG TASVVCLLNN FYPREAKVQW KVDNALQSGN SQESVTEQDS KDSTYLSLST 180
LTLKADYK HKVYACEVTH QGLSSPVTKS FNRGEC 216

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SEQ ID NO: 526          moltype = AA length = 582
FEATURE               Location/Qualifiers
source                1..582
                    mol_type = protein
                    organism = Synthetic construct

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SEQUENCE: 526
EVQLESQGGG LVQPGGSLRL SCVSGGFNFK DYCMTWVRQA PGKGLEWVSA IVYSGGSTYY 60
ADSVKGRPTI SRDNSKNTLY LQMNSLRAED TAVYYCAKYT RGSYFYDAMD VWGQGTTVTV 120
SSASTKGPSV FPLAPCSRST SESTAALGCL VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ 180
SSGLYSLSSV VTPSSSLGT KTYTCNVDPK PSNTKVDKRV ESKYGPPCPP CPAPEFLGGP 240
SVFLFPPKPK DTLMISRTP VTCVVVDVDSQ EDPEVQFNWY VDGVEVHNAK TKPREEQFNS 300
TYRVVSVLTV LHQDWLNGKE YKCKVSNKGL PSSIEKTISK AKGQPREPQV YTLPPSQEEM 360
TKNQVSLTCL VKGFYPSDIA VEWESNGQPE NNYKTTPPVL DSDGSFFLYS RLTVDKSRWQ 420
EGNVFSCSVM HEALHNHYTQ KSLSLSLGKA PTSSTKKTQ LQLEHLLAL QMILNGINNY 480
KNPKLTEMLT FKFYMPKKAT ELKHLQCLEE ELKPLEEVLN LAQSKNFHLR PRDLISINIV 540
IVLELKGSET TFMCEYADET ATIVEFLNRW ITFCQSIIST LT 582

```

```

SEQ ID NO: 527          moltype = AA length = 216
FEATURE               Location/Qualifiers
source                1..216
                    mol_type = protein
                    organism = Synthetic construct

```

```

SEQUENCE: 527
EIVLTQSPGT LSLSPGERAT LSCRASQSIG RSFLAWYQQK PGQAPRLLIY DASTRATDIP 60
DRFSGSGSGT EFTLTISLQ SEDFAVYCYQ QYYDWPPLTF GGGTKVEIKR TVAAPSVFIF 120
PPSDEQLKSG TASVVCLLNN FYPREAKVQW KVDNALQSGN SQESVTEQDS KDSTYLSLST 180
LTLKADYK HKVYACEVTH QGLSSPVTKS FNRGEC 216

```

```

SEQ ID NO: 528          moltype = AA length = 582
FEATURE               Location/Qualifiers
source                1..582
                    mol_type = protein
                    organism = Synthetic construct

```

```

SEQUENCE: 528
EVQLESQGGG LVQPGGSLRL SCVSGGFNFK DYCMTWVRQA PGKGLEWVSA IVYSGGSTYY 60
ADSVKGRPTI SRDNSKNTLY LQMNSLRAED TAVYYCAKYT RGSYFYDAMD VWGQGTTVTV 120
SSASTKGPSV FPLAPCSRST SESTAALGCL VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ 180
SSGLYSLSSV VTPSSSLGT KTYTCNVDPK PSNTKVDKRV ESKYGPPCPP CPAPEFEGGP 240
SVFLFPPKPK DTLMISRTP VTCVVVDVDSQ EDPEVQFNWY VDGVEVHNAK TKPREEQFNS 300
TYRVVSVLTV LHQDWLNGKE YKCKVSNKGL PSSIEKTISK AKGQPREPQV YTLPPSQEEM 360
TKNQVSLTCL VKGFYPSDIA VEWESNGQPE NNYKTTPPVL DSDGSFFLYS RLTVDKSRWQ 420
EGNVFSCSVM HEALHNHYTQ KSLSLSLGKA PASSSTKKTQ LQLEHLLAL QMILNGINNY 480
KNPKLTEMLT FKFYMPKKAT ELKHLQCLEE ELKPLEEVLN LAQSKNFHLR PRDLISINIV 540
IVLELKGSET TFMCEYADET ATIVEFLNRW ITFAQSIIST LT 582

```

```

SEQ ID NO: 529          moltype = AA length = 582
FEATURE               Location/Qualifiers
source                1..582
                    mol_type = protein
                    organism = Synthetic construct

```

```

SEQUENCE: 529
EVQLESQGGG LVQPGGSLRL SCVSGGFNFK DYCMTWVRQA PGKGLEWVSA IVYSGGSTYY 60
ADSVKGRPTI SRDNSKNTLY LQMNSLRAED TAVYYCAKYT RGSYFYDAMD VWGQGTTVTV 120
SSASTKGPSV FPLAPCSRST SESTAALGCL VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ 180
SSGLYSLSSV VTPSSSLGT KTYTCNVDPK PSNTKVDKRV ESKYGPPCPP CPAPEFAGAP 240
SVFLFPPKPK DTLMISRTP VTCVVVDVDSQ EDPEVQFNWY VDGVEVHNAK TKPREEQFNS 300
TYRVVSVLTV LHQDWLNGKE YKCKVSNKGL PSSIEKTISK AKGQPREPQV YTLPPSQEEM 360
TKNQVSLTCL VKGFYPSDIA VEWESNGQPE NNYKTTPPVL DSDGSFFLYS RLTVDKSRWQ 420
EGNVFSCSVM HEALHNHYTQ KSLSLSLGKA PASSSTKKTQ LQLEHLLAL QMILNGINNY 480

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-continued

KNPKLTEMILT FKFYMPKAT ELKHLQCLEE ELKPLEEVLN LAQSKNFHLR PRDLISINIV 540
 IVLELKGSET TFMCEYADET ATIVEFLNRW ITFAQSIIST LT 582

SEQ ID NO: 530 moltype = AA length = 585
 FEATURE Location/Qualifiers
 source 1..585
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 530
 EVQLESGLGG LVQPGGSLRL SCAASGFTFK DYCMTWVRQA PGKGLEWVSA IVYSGGSTYY 60
 ADSVKGRFTI SRDNSKNTLY LQMNLRRAED TAVYYCAKYT RASYFYDAMD VWGQGTTVTV 120
 SSASTKGPSV FPLAPSSKST SGGTAALGCL VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ 180
 SSGLYSLSSV VTPSSSLGT QTYICNVNHHK PSNTKVDKKV EPKSCDKTHT CPPCPAPELL 240
 GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSHEDPEVKF NQYVDGVEVH NAKTKPREEQ 300
 YNSTYRVVSV LTVLHQDWLN GKEYKCKVSN KALPAPIEKT ISKAKGQPRE PQVYTLPPSR 360
 DELTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTT PVLDSGGSFF LYSKLTVDKS 420
 RWQQGNVFSV SVMHEALHNNH YTKQSLSLSP GKAPASSSTK KTQLQLEHLL LALQMILNGI 480
 NNYKNPKLTE MLTFKFYMPK KATELKHLC LEEELKPLEE VLNLAQSKNF HLRPRDLISN 540
 INVIVLELKG SETTFMCEYA DETATIVEFL NRWITFAQSI ISTLT 585

SEQ ID NO: 531 moltype = AA length = 585
 FEATURE Location/Qualifiers
 source 1..585
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 531
 EVQLESGLGG LVQPGGSLRL SCAASGFTFK DYCMTWVRQA PGKGLEWVSA IVYSGGSTYY 60
 ADSVKGRFTI SRDNSKNTLY LQMNLRRAED TAVYYCAKYT RASYFYDAMD VWGQGTTVTV 120
 SSASTKGPSV FPLAPSSKST SGGTAALGCL VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ 180
 SSGLYSLSSV VTPSSSLGT QTYICNVNHHK PSNTKVDKKV EPKSCDKTHT CPPCPAPELE 240
 GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSHEDPEVKF NQYVDGVEVH NAKTKPREEQ 300
 YNSTYRVVSV LTVLHQDWLN GKEYKCKVSN KALPAPIEKT ISKAKGQPRE PQVYTLPPSR 360
 DELTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTT PVLDSGGSFF LYSKLTVDKS 420
 RWQQGNVFSV SVMHEALHNNH YTKQSLSLSP GKAPASSSTK KTQLQLEHLL LALQMILNGI 480
 NNYKNPKLTE MLTFKFYMPK KATELKHLC LEEELKPLEE VLNLAQSKNF HLRPRDLISN 540
 INVIVLELKG SETTFMCEYA DETATIVEFL NRWITFAQSI ISTLT 585

SEQ ID NO: 532 moltype = AA length = 585
 FEATURE Location/Qualifiers
 source 1..585
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 532
 EVQLESGLGG LVQPGGSLRL SCAASGFTFK SYAMHWVRQA PGKGLEWVSA IVYSGGSTYY 60
 ADSVKGRFTI SRDNSKNTLY LQMNLRRAED TAVYYCAKYD RASYFYDAMD VWGQGTTVTV 120
 SSASTKGPSV FPLAPSSKST SGGTAALGCL VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ 180
 SSGLYSLSSV VTPSSSLGT QTYICNVNHHK PSNTKVDKKV EPKSCDKTHT CPPCPAPELA 240
 GAPSVFLFPP KPKDTLMISR TPEVTCVVVD VSHEDPEVKF NQYVDGVEVH NAKTKPREEQ 300
 YNSTYRVVSV LTVLHQDWLN GKEYKCKVSN KALPAPIEKT ISKAKGQPRE PQVYTLPPSR 360
 DELTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTT PVLDSGGSFF LYSKLTVDKS 420
 RWQQGNVFSV SVMHEALHNNH YTKQSLSLSP GKAPASSSTK KTQLQLEHLL LALQMILNGI 480
 NNYKNPKLTE MLTFKFYMPK KATELKHLC LEEELKPLEE VLNLAQSKNF HLRPRDLISN 540
 INVIVLELKG SETTFMCEYA DETATIVEFL NRWITFAQSI ISTLT 585

SEQ ID NO: 533 moltype = AA length = 585
 FEATURE Location/Qualifiers
 source 1..585
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 533
 EVQLESGLGG LVQPGGSLRL SCAASGFTFK DYCMTWVRQA PGKGLEWVSA IVYSGGSTYY 60
 ADSVKGRFTI SRDNSKNTLY LQMNLRRAED TAVYYCAKYT RASYFYDAMD VWGQGTTVTV 120
 SSASTKGPSV FPLAPSSKST SGGTAALGCL VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ 180
 SSGLYSLSSV VTPSSSLGT QTYICNVNHHK PSNTKVDKKV EPKSCDKTHT CPPCPAPELE 240
 GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSHEDPEVKF NQYVDGVEVH NAKTKPREEQ 300
 YNSTYRVVSV LTVLHQDWLN GKEYKCKVSN KALPAPIEKT ISKAKGQPRE PQVYTLPPSR 360
 DELTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTTT PVLDSGGSFF LYSKLTVDKS 420
 RWQQGNVFSV SVMHEALHNNH YTKQSLSLSP GKAPASSSTK KTQLQLEHLL LALQMILNGI 480
 NNYKNPKLTE MLTFKFYMPK KATELKHLC LEEELKPLEE VLNLAQSKNF HLRPRDLISN 540
 INVIVLELKG SETTFMCEYA DETATIVEFL NRWITFAQSI ISTLT 585

SEQ ID NO: 534 moltype = AA length = 582
 FEATURE Location/Qualifiers
 source 1..582
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 534
 EVQLESGLGG LVQPGGSLRL SCAASGFTFK DYCMTWVRQA PGKGLEWVSA IVYSGGSTYY 60
 ADSVKGRFTI SRDNSKNTLY LQMNLRRAED TAVYYCAKYT RASYFYDAMD VWGQGTTVTV 120

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| | | | | | | |
|------------|------------|------------|------------|------------|------------|-----|
| SSASTKGPSV | FPLAPCSRST | SESTAALGCL | VKDYPPEPVT | VSWNSGALTS | GVHTFPAVLQ | 180 |
| SSGLYSLSSV | VTVPSSSLGT | KTYTCNVDPK | PSNTKVDKRV | ESKYGPPCPP | CPAPEFLGGP | 240 |
| SVFLFPPKPK | DTLMISRTP | VTCVVVDVSD | EDPEVQFNWY | VDGVEVHNAK | TKPREEQFNS | 300 |
| TYRVVSVLTV | LHQDWLNGKE | YKCKVSNKGL | PSSIEKTISK | AKGQPREPQV | YTLPPSQEEM | 360 |
| TKNQVSLTCL | VKGFYPSDIA | VEWESNGQPE | NNYKTTTPVL | DSDGSFFLYS | RLTVDKSRWQ | 420 |
| EGNVFSCSVM | HEALHNHYTQ | KSLSLSLGKA | PASSSTKKTQ | LQLEHLLDL | QMILNGINNY | 480 |
| KNPKLTEMLT | FKFYMPKKAT | ELKHLQCLEE | ELKPLEEVLN | LAQSKNFHLR | PRKLISNINV | 540 |
| IVLELKGSET | TFMCEYADET | ATIVEFLNRW | ITFAQSIIST | LT | | 582 |

SEQ ID NO: 535 moltype = AA length = 585
 FEATURE Location/Qualifiers
 source 1..585
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 535

| | | | | | | | |
|------------|------------|------------|------------|------------|------------|------------|-----|
| EVQLES | GGGG | LVQPGGSLRL | SCAASGFTFK | DYCMTWVRQA | PGKGLEWVSA | IVYSGGSTYY | 60 |
| ADSVKGRFTI | SRDNSKNTLY | LQMNLRRAED | TAVYYCAKYT | RASYFYDAMD | VWGQGTTVTV | | 120 |
| SSASTKGPSV | FPLAPSSKST | SGGTAALGCL | VKDYPPEPVT | VSWNSGALTS | GVHTFPAVLQ | | 180 |
| SSGLYSLSSV | VTVPSSSLGT | QTYICNVNKH | PSNTKVDKRV | EPKSCDKTHT | CPPCPAPELL | | 240 |
| GGPSVFLFPP | KPKDTLMISR | TPEVTCVVVD | VSHEDPEVKF | NWYVDGVEVH | NAKTKPREEQ | | 300 |
| YNSTYRVVSV | LTVLHQDWLN | GKEYKCKVSN | KALPAPIEKT | ISKAKGQPRE | PQVYTLPPSR | | 360 |
| DELTKNQVSL | TCLVKGFYPS | DIAVEWESNG | QPENNYKTTT | PVLDSGGSFF | LYSKLTVDKS | | 420 |
| RWQQGNVFS | SVMHEALHNH | YTQKSLSLSP | GKAPASSSTK | KTQLQLEHLL | LDLQMLNGI | | 480 |
| NNYKNPKLTE | MLTFKFMYPK | KATELKHLC | LEELKPLEE | VLNLAQSKNF | HLRPRDLISN | | 540 |
| INVKLELKG | SETTFMCEYA | DETATIVEFL | NRWITFAQSI | ISTLT | | | 585 |

SEQ ID NO: 536 moltype = AA length = 585
 FEATURE Location/Qualifiers
 source 1..585
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 536

| | | | | | | | |
|------------|------------|------------|------------|------------|------------|------------|-----|
| EVQLES | GGGG | LVQPGGSLRL | SCAASGFTFK | DYCMTWVRQA | PGKGLEWVSA | IVYSGGSTYY | 60 |
| ADSVKGRFTI | SRDNSKNTLY | LQMNLRRAED | TAVYYCAKYT | RASYFYDAMD | VWGQGTTVTV | | 120 |
| SSASTKGPSV | FPLAPSSKST | SGGTAALGCL | VKDYPPEPVT | VSWNSGALTS | GVHTFPAVLQ | | 180 |
| SSGLYSLSSV | VTVPSSSLGT | QTYICNVNKH | PSNTKVDKRV | EPKSCDKTHT | CPPCPAPELE | | 240 |
| GGPSVFLFPP | KPKDTLMISR | TPEVTCVVVD | VSHEDPEVKF | NWYVDGVEVH | NAKTKPREEQ | | 300 |
| YNSTYRVVSV | LTVLHQDWLN | GKEYKCKVSN | KALPAPIEKT | ISKAKGQPRE | PQVYTLPPSR | | 360 |
| DELTKNQVSL | TCLVKGFYPS | DIAVEWESNG | QPENNYKTTT | PVLDSGGSFF | LYSKLTVDKS | | 420 |
| RWQQGNVFS | SVMHEALHNH | YTQKSLSLSP | GKAPASSSTK | KTQLQLEHLL | LDLQMLNGI | | 480 |
| NNYKNPKLTE | MLTFKFMYPK | KATELKHLC | LEELKPLEE | VLNLAQSKNF | HLRPRDLISN | | 540 |
| INVKLELKG | SETTFMCEYA | DETATIVEFL | NRWITFAQSI | ISTLT | | | 585 |

SEQ ID NO: 537 moltype = AA length = 582
 FEATURE Location/Qualifiers
 source 1..582
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 537

| | | | | | | | |
|------------|------------|------------|------------|------------|------------|------------|-----|
| EVQLES | GGGG | LVQPGGSLRL | SCAASGFTFK | DYCMTWVRQA | PGKGLEWVSA | IVYSGGSTYY | 60 |
| ADSVKGRFTI | SRDNSKNTLY | LQMNLRRAED | TAVYYCAKYT | RASYFYDAMD | VWGQGTTVTV | | 120 |
| SSASTKGPSV | FPLAPCSRST | SESTAALGCL | VKDYPPEPVT | VSWNSGALTS | GVHTFPAVLQ | | 180 |
| SSGLYSLSSV | VTVPSSSLGT | KTYTCNVDPK | PSNTKVDKRV | ESKYGPPCPP | CPAPEFLGGP | | 240 |
| SVFLFPPKPK | DTLMISRTP | VTCVVVDVSD | EDPEVQFNWY | VDGVEVHNAK | TKPREEQFNS | | 300 |
| TYRVVSVLTV | LHQDWLNGKE | YKCKVSNKGL | PSSIEKTISK | AKGQPREPQV | YTLPPSQEEM | | 360 |
| TKNQVSLTCL | VKGFYPSDIA | VEWESNGQPE | NNYKTTTPVL | DSDGSFFLYS | RLTVDKSRWQ | | 420 |
| EGNVFSCSVM | HEALHNHYTQ | KSLSLSLGKA | PASSSTKKTQ | LQLEHLLDL | QMILNGINNY | | 480 |
| KNPKLTEMLT | FKFYMPKKAT | ELKHLQCLEE | ELKPLEEVLN | LAQSKNFHLR | PRDLISNINV | | 540 |
| KVLELKGSET | TFMCEYADET | ATIVEFLNRW | ITFAQSIIST | LT | | | 582 |

SEQ ID NO: 538 moltype = AA length = 585
 FEATURE Location/Qualifiers
 source 1..585
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 538

| | | | | | | | |
|------------|------------|------------|------------|------------|------------|------------|-----|
| EVQLES | GGGG | LVQPGGSLRL | SCAASGFTFK | DYCMTWVRQA | PGKGLEWVSA | IVYSGGSTYY | 60 |
| ADSVKGRFTI | SRDNSKNTLY | LQMNLRRAED | TAVYYCAKYT | RASYFYDAMD | VWGQGTTVTV | | 120 |
| SSASTKGPSV | FPLAPSSKST | SGGTAALGCL | VKDYPPEPVT | VSWNSGALTS | GVHTFPAVLQ | | 180 |
| SSGLYSLSSV | VTVPSSSLGT | QTYICNVNKH | PSNTKVDKRV | EPKSCDKTHT | CPPCPAPELA | | 240 |
| GAPSVFLFPP | KPKDTLMISR | TPEVTCVVVD | VSHEDPEVKF | NWYVDGVEVH | NAKTKPREEQ | | 300 |
| YNSTYRVVSV | LTVLHQDWLN | GKEYKCKVSN | KALPAPIEKT | ISKAKGQPRE | PQVYTLPPSR | | 360 |
| DELTKNQVSL | TCLVKGFYPS | DIAVEWESNG | QPENNYKTTT | PVLDSGGSFF | LYSKLTVDKS | | 420 |
| RWQQGNVFS | SVMHEALHNH | YTQKSLSLSP | GKAPASSSTK | KTQLQLEHLL | LSLQMLNGI | | 480 |
| NNYKNPKLTE | MLTFKFMYPK | KATELKHLC | LEELKPLEE | VLNLAQSKNF | HLRPRDLISN | | 540 |
| INVIVLELKG | SETTFMCEYA | DETATIVEFL | NRWITFAQSI | ISTLT | | | 585 |

SEQ ID NO: 539 moltype = AA length = 585
 FEATURE Location/Qualifiers

-continued

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source                1..585
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 539
EVQLESSEGGG LVQPGGSLRL SCAASGFTFK DYCMTWVRQA PGKGLEWVSA IVYSGGSTYY 60
ADSVKGRFTI SRDNSKNTLY LQMNLRRAED TAVYYCAKYT RASYFYDAMD VWGQGTTVTV 120
SSASTKGPSV FPLAPSSKST SGGTAALGCL VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ 180
SSGLYSLSV VTPSSSLGT QTYICNVNHHK PSNTKVDKKV EPKSCDKTHT CPPCPAPELA 240
GAPSVFLFPP KPKDTLMISR TPEVTCVVVD VSHEDPEVKF NQYVDGVEVH NAKTKPREEQ 300
YNSTYRVVSV LTVLHQDWLNL GKEYKCKVSN KALPAPIEKT ISKAKGQPRE PQVYTLPPSR 360
DELTKNQVSL TCVLKGFYPS DIAVEWESNG QPENNYKTTT PVLDSGGSFF LYSKLTVDKS 420
RWQQGNVFSV SVMHEALHNNH YTKQSLSLSP GKAPASSSTK KTQLQLEHLL LDLQMILNGI 480
NNYKNPKLTE MLTFKFMYPK KATELKHLCQ LEEELKPLEE VLNLQAQSKNF HLRPRDLISN 540
INVIVLELKG SETTFMCEYA DETATIVEFL NRWITFAQSI ISTLT 585

SEQ ID NO: 540        moltype = AA length = 585
FEATURE              Location/Qualifiers
source                1..585
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 540
EVQLESSEGGG LVQPGGSLRL SCAASGFTFK DYCMTWVRQA PGKGLEWVSA IVYSGGSTYY 60
ADSVKGRFTI SRDNSKNTLY LQMNLRRAED TAVYYCAKYT RASYFYDAMD VWGQGTTVTV 120
SSASTKGPSV FPLAPSSKST SGGTAALGCL VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ 180
SSGLYSLSV VTPSSSLGT QTYICNVNHHK PSNTKVDKKV EPKSCDKTHT CPPCPAPELA 240
GAPSVFLFPP KPKDTLMISR TPEVTCVVVD VSHEDPEVKF NQYVDGVEVH NAKTKPREEQ 300
YNSTYRVVSV LTVLHQDWLNL GKEYKCKVSN KALPAPIEKT ISKAKGQPRE PQVYTLPPSR 360
DELTKNQVSL TCVLKGFYPS DIAVEWESNG QPENNYKTTT PVLDSGGSFF LYSKLTVDKS 420
RWQQGNVFSV SVMHEALHNNH YTKQSLSLSP GKAPASSSTK KTQLQLEHLL LDLQMILNGI 480
NNYKNPKLTE MLTFKFMYPK KATELKHLCQ LEEELKPLEE VLNLQAQSKNF HLRPRDLISN 540
INVIVLELKG SETTFMCEYA DETATIVEFL NRWITFAQSI ISTLT 585

SEQ ID NO: 541        moltype = AA length = 585
FEATURE              Location/Qualifiers
source                1..585
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 541
EVQLESSEGGG LVQPGGSLRL SCAASGFTFK DYCMTWVRQA PGKGLEWVSA IVYSGGSTYY 60
ADSVKGRFTI SRDNSKNTLY LQMNLRRAED TAVYYCAKYT RASYFYDAMD VWGQGTTVTV 120
SSASTKGPSV FPLAPSSKST SGGTAALGCL VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ 180
SSGLYSLSV VTPSSSLGT QTYICNVNHHK PSNTKVDKKV EPKSCDKTHT CPPCPAPELA 240
GAPSVFLFPP KPKDTLMISR TPEVTCVVVD VSHEDPEVKF NQYVDGVEVH NAKTKPREEQ 300
YNSTYRVVSV LTVLHQDWLNL GKEYKCKVSN KALPAPIEKT ISKAKGQPRE PQVYTLPPSR 360
DELTKNQVSL TCVLKGFYPS DIAVEWESNG QPENNYKTTT PVLDSGGSFF LYSKLTVDKS 420
RWQQGNVFSV SVMHEALHNNH YTKQSLSLSP GKAPASSSTK KTQLQLEHLL LDLQMILNGI 480
NNYKNPKLTE MLTFKFMYPK KATELKHLCQ LEEELKPLEE VLNLQAQSKNF HLRPRDLISN 540
INVEVLELKG SETTFMCEYA DETATIVEFL NRWITFAQSI ISTLT 585

SEQ ID NO: 542        moltype = AA length = 585
FEATURE              Location/Qualifiers
source                1..585
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 542
EVQLESSEGGG LVQPGGSLRL SCAASGFTFK DYCMTWVRQA PGKGLEWVSA IVYSGGSTYY 60
ADSVKGRFTI SRDNSKNTLY LQMNLRRAED TAVYYCAKYT RASYFYDAMD VWGQGTTVTV 120
SSASTKGPSV FPLAPSSKST SGGTAALGCL VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ 180
SSGLYSLSV VTPSSSLGT QTYICNVNHHK PSNTKVDKKV EPKSCDKTHT CPPCPAPELA 240
GAPSVFLFPP KPKDTLMISR TPEVTCVVVD VSHEDPEVKF NQYVDGVEVH NAKTKPREEQ 300
YNSTYRVVSV LTVLHQDWLNL GKEYKCKVSN KALPAPIEKT ISKAKGQPRE PQVYTLPPSR 360
DELTKNQVSL TCVLKGFYPS DIAVEWESNG QPENNYKTTT PVLDSGGSFF LYSKLTVDKS 420
RWQQGNVFSV SVMHEALHNNH YTKQSLSLSP GKAPASSSTK KTQLQLEHLL LDLQMILNGI 480
NNYKNPKLTE MLTFKFMYPK KATELKHLCQ LEEELKPLEE VLNLQAQSKNF HLRPRDLISN 540
INVSLELKG SETTFMCEYA DETATIVEFL NRWITFAQSI ISTLT 585

SEQ ID NO: 543        moltype = AA length = 585
FEATURE              Location/Qualifiers
source                1..585
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 543
EVQLESSEGGG LVQPGGSLRL SCAASGFTFK DYCMTWVRQA PGKGLEWVSA IVYSGGSTYY 60
ADSVKGRFTI SRDNSKNTLY LQMNLRRAED TAVYYCAKYT RASYFYDAMD VWGQGTTVTV 120
SSASTKGPSV FPLAPSSKST SGGTAALGCL VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ 180
SSGLYSLSV VTPSSSLGT QTYICNVNHHK PSNTKVDKKV EPKSCDKTHT CPPCPAPELA 240
GAPSVFLFPP KPKDTLMISR TPEVTCVVVD VSHEDPEVKF NQYVDGVEVH NAKTKPREEQ 300
YNSTYRVVSV LTVLHQDWLNL GKEYKCKVSN KALPAPIEKT ISKAKGQPRE PQVYTLPPSR 360
DELTKNQVSL TCVLKGFYPS DIAVEWESNG QPENNYKTTT PVLDSGGSFF LYSKLTVDKS 420

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RWQQGNVFSV SVMHEALHNNH YTKQSLSLSP GKAPASSSTK KTQLQLEHLL LDLQMILNGI 480
NNYKNPKLTE MLTFKFMYPK KATELKHLC LEEELKPLEE VLNLAQSKNF HLRPRDLISN 540
INVIVLELKG SETTFMCEYA DETATIVEFL NRWITFAQSI ISTLT 585

```

```

SEQ ID NO: 544      moltype = AA length = 585
FEATURE            Location/Qualifiers
source             1..585
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 544
EVQLLESQGGG LVQPQGSRLR SCAASGFTFK DYCMTWVRQA PGKGLEWVSA IVYSGGSTYY 60
ADSVKGRFTI SRDNSKNTLY LQMNNLRRAED TAVYYCAKYT RASYFYDAMD VWGQGTFTVT 120
SSASTKGPSV FPLAPSSKST SGGTAALGCL VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ 180
SSGLYSLSSV VTPVSSSLGT QTYICNVNHHK PSNTKVDKVK EPKSCDKTHT CPPCPAPELA 240
GAPSVFLFPP KPKDTLMLSR TPEVTCVVVD VSHEDPEVKF NWYVDGVEVH NAKTKPREEQ 300
YNSTYRVVSV LTVLHQDWLNL GKEYKCKVSN KALPAPIEKT ISKAKGQPRE PQVYTLPPSR 360
DELTKNQVSL TCVLKGFYPS DIAVEWESNG QPENNYKTTT PVLDSGDSFF LYSKLTVDKS 420
RWQQGNVFSV SVMHEALHNNH YTKQSLSLSP GKAPASSSTK KTQLQLEELL LDLQMILNGI 480
NNYKNPKLTE MLTFKFMYPK KATELKHLC LEEELKPLEE VLNLAQSKNF HLRPRDLISN 540
INVIVLELKG SETTFMCEYA DETATIVEFL NRWITFAQSI ISTLT 585

```

```

SEQ ID NO: 545      moltype = AA length = 586
FEATURE            Location/Qualifiers
source             1..586
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 545
EVQLVESGGG LVQPGRSLKL SCAVSGFTFS DYAMAWVRQA PKKGLEWVAT ISYDGSRTYY 60
RDSVKGRFTI SRDNAKITLY LQMDLSLRSR TATYYCARHG SGYFDYWGQG VMVTVSSAST 120
KGPSVFLPAP SSKSTSGGTA ALGCLVKDYF PEPVTVSWNS GALTSGVHTF PAVLQSSGLY 180
SLSSVVTVPS SSLGTQTYIC NVNHKPSNTK VDKKVEPKSC DKHTCTPPCP APELLGGPSV 240
FLFPPKPKDT LMIKRTPEVT CVVVDVSHED PEVKFNWYVD GVEVHNAKTK PREEQYNSTY 300
RVVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK GQPREPQVYV LPPSRDELTK 360
NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTTPVLDL DGSFFLYSKL TVDKSRWQQG 420
NVFSCSVME ALHNHYTQKS LSLSPGKSGG GGSAPASSST KKTQLQLEHL LALQMILNG 480
INNYKNPKLT EMLTFKFMYP KKATELKHLC LEEELKPLEE EVLNLAQSKN FHLRPRDLIS 540
NINIVLELKG SETTFMCEY ADETATIVEFL LNRWITFAQS IISTLT 586

```

```

SEQ ID NO: 546      moltype = AA length = 580
FEATURE            Location/Qualifiers
source             1..580
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 546
EVQLVESGGG LVQPGRSLKL SCAVSGFTFS DYAMAWVRQA PKKGLEWVAT ISYDGSRTYY 60
RDSVKGRFTI SRDNAKITLY LQMDLSLRSR TATYYCARHG SGYFDYWGQG VMVTVSSAST 120
KGPSVFLPAP SSKSTSGGTA ALGCLVKDYF PEPVTVSWNS GALTSGVHTF PAVLQSSGLY 180
SLSSVVTVPS SSLGTQTYIC NVNHKPSNTK VDKKVEPKSC DKHTCTPPCP APELLGGPSV 240
FLFPPKPKDT LMIKRTPEVT CVVVDVSHED PEVKFNWYVD GVEVHNAKTK PREEQYNSTY 300
RVVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK GQPREPQVYV LPPSRDELTK 360
NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTTPVLDL DGSFFLYSKL TVDKSRWQQG 420
NVFSCSVME ALHNHYTQKS LSLSPGKAPA SSSTKKTQLQ LEHLLELALQML INGINNYKN 480
PKLTEMLETFK FYPMPKATEL KHLQCLEEEL KPLEEVLNLA QSKNFHLRPR DLISNINIV 540
LELKGSETTF MCEYADETAT IVEFLNRWIT FAQSIISTLT 580

```

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SEQ ID NO: 547      moltype = AA length = 447
FEATURE            Location/Qualifiers
source             1..447
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 547
QVQLVQSGSE LKPKGASVKV SCKASGYSLY GTSMHWRQA PGQGLEWVMG ISPFTGRATY 60
AQQFTGRFV FSLDTSVSTAY LQISSLKAED TAVYYCARDY DRYYYAMDY WQQGTFTVTS 120
SASTKGPSVF PLAPCSRSTS ESTAALGCLV KDYFPEPVTV SWNSGALTSV VHTFPAVLQS 180
SGLYSLSSVV TVPSSSLGK TYTCNVDHK PSNTKVDKRV SKYGPCCPPC PAPEFEGGPS 240
VFLFPPKPKD TLMISRTPEV TCVVVDVDSQ EPEVQFNWYV DGVVHNAKT KPREEQFNST 300
YRVVSVLTVL HQDWLNGKEY CKVSNKGLP SIEKTISKA KGQPREPQVY TLPPSQEEMT 360
KNQVSLTCLV KGFYPSDIAV EWESNGQPEN NYKTTTPVLD SDGSFFLYSR LTVDKSRWQE 420
GNVFSVSMH EALHNHYTQK SLSLSLG 447

```

```

SEQ ID NO: 548      moltype = AA length = 447
FEATURE            Location/Qualifiers
source             1..447
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 548
QVQLVQSGSE LKPKGASVKV SCKASGYSLY GTSMHWRQA PGQGLEWVMG ISPFTGRATY 60
AQQFTGRFV FSLDTSVSTAY LQISSLKAED TAVYYCARDY DRYYYAMDY WQQGTFTVTS 120
SASTKGPSVF PLAPCSRSTS ESTAALGCLV KDYFPEPVTV SWNSGALTSV VHTFPAVLQS 180

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SGLYSLSSVV TVPSSSLGTK TYTCNVDPK SNTKVDKRV SKYGPPCPPC PAPEFAGAPS 240
VFLFPPKPKD TLMISRTPV TCVVVDVQS DPEVQFNWYV DGVEVHNAKT KPREEQFNST 300
YRVVSVLTVL HQDWLNGKEY KCKVSNKGLP SSIIEKTISKA KGQPREPQVY TLPSSQEEMT 360
KNQVSLTCLV KGFYPSDIAV EWESNGQPEN NYKTTTPVLD SDGSFFLYSR LTVDKSRWQE 420
GNVFSVSMH EALHNHYTQK SLSLSLG 447

```

```

SEQ ID NO: 549      moltype = AA length = 447
FEATURE           Location/Qualifiers
source            1..447
                  mol_type = protein
                  organism = Synthetic construct

```

```

SEQUENCE: 549
QVQLVQSGSE LKKPGASVKV SCKASGYSLY GTSMHWVRQA PGQGLEWGMG ISPFTGRATY 60
AQQFTGRFVF SLDTSVSTAY LQISSLKAED TAVYYCARDY DYRYYYAMDY WQQGTTVTVS 120
SASTKGPSVF PLAPCSRSTS ESTAALGCLV KDYPPEPVTV SWNSGALTSV VHTFPAVLQS 180
SGLYSLSSVV TVPSSSLGTK TYTCNVDPK SNTKVDKRV SKYGPPCPPC PAPEFEGGGS 240
VFLFPPKPKD TLMISRTPV TCVVVDVQS DPEVQFNWYV DGVEVHNAKT KPREEQFNST 300
YRVVSVLTVL HQDWLNGKEY KCKVSNKGLP SSIIEKTISKA KGQPREPQVY TLPSSQEEMT 360
KNQVSLTCLV KGFYPSDIAV EWESNGQPEN NYKTTTPVLD SDGSFFLYSR LTVDKSRWQE 420
GNVFSVSMH EALHNHYTQK SLSLSLG 447

```

```

SEQ ID NO: 550      moltype = AA length = 581
FEATURE           Location/Qualifiers
source            1..581
                  mol_type = protein
                  organism = Synthetic construct

```

```

SEQUENCE: 550
QVQLVQSGSE LKKPGASVKV SCKASGYSLY GTSMHWVRQA PGQGLEWGMG ISPFTGRATY 60
AQQFTGRFVF SLDTSVSTAY LQISSLKAED TAVYYCARDY DYRYYYAMDY WQQGTTVTVS 120
SASTKGPSVF PLAPCSRSTS ESTAALGCLV KDYPPEPVTV SWNSGALTSV VHTFPAVLQS 180
SGLYSLSSVV TVPSSSLGTK TYTCNVDPK SNTKVDKRV SKYGPPCPPC PAPEFLGGPS 240
VFLFPPKPKD TLMISRTPV TCVVVDVQS DPEVQFNWYV DGVEVHNAKT KPREEQFNST 300
YRVVSVLTVL HQDWLNGKEY KCKVSNKGLP SSIIEKTISKA KGQPREPQVY TLPSSQEEMT 360
KNQVSLTCLV KGFYPSDIAV EWESNGQPEN NYKTTTPVLD SDGSFFLYSR LTVDKSRWQE 420
GNVFSVSMH EALHNHYTQK SLSLSLGKAP ASSSTKKTQL QLEHLLALQ MILNGINNYK 480
NPKLTEMLETF KFYMPKKATE LKHLQCLEEE LKPLEEVLNL AQSKNFHLRP RDLISININVI 540
VLELKGSETT  FMCYADETA TIVEFLNRWI TFAQSIISTL T 581

```

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SEQ ID NO: 551      moltype = AA length = 581
FEATURE           Location/Qualifiers
source            1..581
                  mol_type = protein
                  organism = Synthetic construct

```

```

SEQUENCE: 551
QVQLVQSGSE LKKPGASVKV SCKASGYSLY GTSMHWVRQA PGQGLEWGMG ISPFTGRATY 60
AQQFTGRFVF SLDTSVSTAY LQISSLKAED TAVYYCARDY DYRYYYAMDY WQQGTTVTVS 120
SASTKGPSVF PLAPCSRSTS ESTAALGCLV KDYPPEPVTV SWNSGALTSV VHTFPAVLQS 180
SGLYSLSSVV TVPSSSLGTK TYTCNVDPK SNTKVDKRV SKYGPPCPPC PAPEFEGGGS 240
VFLFPPKPKD TLMISRTPV TCVVVDVQS DPEVQFNWYV DGVEVHNAKT KPREEQFNST 300
YRVVSVLTVL HQDWLNGKEY KCKVSNKGLP SSIIEKTISKA KGQPREPQVY TLPSSQEEMT 360
KNQVSLTCLV KGFYPSDIAV EWESNGQPEN NYKTTTPVLD SDGSFFLYSR LTVDKSRWQE 420
GNVFSVSMH EALHNHYTQK SLSLSLGKAP ASSSTKKTQL QLEHLLALQ MILNGINNYK 480
NPKLTEMLETF KFYMPKKATE LKHLQCLEEE LKPLEEVLNL AQSKNFHLRP RDLISININVI 540
VLELKGSETT  FMCYADETA TIVEFLNRWI TFAQSIISTL T 581

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SEQ ID NO: 552      moltype = AA length = 441
FEATURE           Location/Qualifiers
source            1..441
                  mol_type = protein
                  organism = Synthetic construct

```

```

SEQUENCE: 552
DVQLVESGGG LVQPGGSLRL SCAASGFTFD ISAMSWVRQA PGKGLEWVST ISGSAYSTYY 60
ADSVKGRFTI SRDNSKSTLY LQMNSLRAED TAVYYCAREI FSDYWGGLTGL VTVSSASTKG 120
PSVFLAPLPC RSTSESTAAL GCLVKDYFPE PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL 180
SSVTVPSST LGTKTYTCNV DHKPSNTKVD KRVESKYGPP CPPCPAPEFE GGPSVFLFPP 240
KPKDTLMSR TPEVTCVVVD VSQEDPEVQF NWWYDVGVEVH NAKTKPREEQ FNSTYRVVSV 300
LTVLHQDWLNL GKEYKCKVSN KGLPSSIEKT ISKAKGQPRE PQVYTLPPSQ EEMTKNIVSL 360
TCLVKGFYPS DIAVEWESNG QPENNYKTP PVLDSGDSFF LYSRLTVDKS RWQEGNVFSC 420
SVMHEALHNH YTQKSLSLSL G 441

```

```

SEQ ID NO: 553      moltype = AA length = 441
FEATURE           Location/Qualifiers
source            1..441
                  mol_type = protein
                  organism = Synthetic construct

```

```

SEQUENCE: 553
DVQLVESGGG LVQPGGSLRL SCAASGFTFD ISAMSWVRQA PGKGLEWVST ISGSAYSTYY 60
ADSVKGRFTI SRDNSKSTLY LQMNSLRAED TAVYYCAREI FSDYWGGLTGL VTVSSASTKG 120
PSVFLAPLPC RSTSESTAAL GCLVKDYFPE PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL 180

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SSVVTVPSS LGTKTYTCNV DHKPSNTKVD KRVESKYGPP CPPCPAPEFA GAPSFLFPP 240
KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWYVDGVEVH NAKTKPREEQ FNSTYRVVSV 300
LTVLHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQPRE PQVYTLPPSQ EEMTKNQVSL 360
TCLVKGFYPS DIAVEWESNG QPENNYKTTT PVLDSGGSFF LYSRLTVDKS RWQEGNVFSC 420
SVMHEALHNN YTQKSLSLSL G 441

```

```

SEQ ID NO: 554      moltype = AA length = 441
FEATURE           Location/Qualifiers
source            1..441
                  mol_type = protein
                  organism = Synthetic construct

```

```

SEQUENCE: 554
DVQLVESGGG LVQPGGSLRL SCAASGFTFD ISAMSWVRQA PGKGLEWVST ISGSAYSTYY 60
ADSVKGRFTI SRDNSKSTLY LQMNSLRAED TAVYYCAREI FSDYWGGLTGL VTVSSASTKG 120
PSVFLAPCS RSTSESTAAL GCLVKDYFPE PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL 180
SSVVTVPSS LGTKTYTCNV DHKPSNTKVD KRVESKYGPP CPPCPAPEFE GGPSVFLFPP 240
KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWYVDGVEVH NAKTKPREEQ FNSTYRVVSV 300
LTVLHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQPRE PQVYTLPPSQ EEMTKNQVSL 360
TCLVKGFYPS DIAVEWESNG QPENNYKTTT PVLDSGGSFF LYSRLTVDKS RWQEGNVFSC 420
SVMHEALHNN YTQKSLSLSL G 441

```

```

SEQ ID NO: 555      moltype = AA length = 575
FEATURE           Location/Qualifiers
source            1..575
                  mol_type = protein
                  organism = Synthetic construct

```

```

SEQUENCE: 555
DVQLVESGGG LVQPGGSLRL SCAASGFTFD ISAMSWVRQA PGKGLEWVST ISGSAYSTYY 60
ADSVKGRFTI SRDNSKSTLY LQMNSLRAED TAVYYCAREI FSDYWGGLTGL VTVSSASTKG 120
PSVFLAPCS RSTSESTAAL GCLVKDYFPE PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL 180
SSVVTVPSS LGTKTYTCNV DHKPSNTKVD KRVESKYGPP CPPCPAPEFL GGPSVFLFPP 240
KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWYVDGVEVH NAKTKPREEQ FNSTYRVVSV 300
LTVLHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQPRE PQVYTLPPSQ EEMTKNQVSL 360
TCLVKGFYPS DIAVEWESNG QPENNYKTTT PVLDSGGSFF LYSRLTVDKS RWQEGNVFSC 420
SVMHEALHNN YTQKSLSLSL GKAPASSSTK KTQLQLEHLL LALQMILNGI NNYKNPKLTE 480
MLTFKFMYPK KATELKHLC LEEELKPLEE VLNLAQSKNF HLRPRDLISN INVIVLELKG 540
SETTFMCEYA DETATIVEFL NRWITFAQSI ISTLT 575

```

```

SEQ ID NO: 556      moltype = AA length = 575
FEATURE           Location/Qualifiers
source            1..575
                  mol_type = protein
                  organism = Synthetic construct

```

```

SEQUENCE: 556
DVQLVESGGG LVQPGGSLRL SCAASGFTFD ISAMSWVRQA PGKGLEWVST ISGSAYSTYY 60
ADSVKGRFTI SRDNSKSTLY LQMNSLRAED TAVYYCAREI FSDYWGGLTGL VTVSSASTKG 120
PSVFLAPCS RSTSESTAAL GCLVKDYFPE PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL 180
SSVVTVPSS LGTKTYTCNV DHKPSNTKVD KRVESKYGPP CPPCPAPEFE GGPSVFLFPP 240
KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWYVDGVEVH NAKTKPREEQ FNSTYRVVSV 300
LTVLHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQPRE PQVYTLPPSQ EEMTKNQVSL 360
TCLVKGFYPS DIAVEWESNG QPENNYKTTT PVLDSGGSFF LYSRLTVDKS RWQEGNVFSC 420
SVMHEALHNN YTQKSLSLSL GKAPASSSTK KTQLQLEHLL LALQMILNGI NNYKNPKLTE 480
MLTFKFMYPK KATELKHLC LEEELKPLEE VLNLAQSKNF HLRPRDLISN INVIVLELKG 540
SETTFMCEYA DETATIVEFL NRWITFAQSI ISTLT 575

```

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SEQ ID NO: 557      moltype = AA length = 575
FEATURE           Location/Qualifiers
source            1..575
                  mol_type = protein
                  organism = Synthetic construct

```

```

SEQUENCE: 557
DVQLVESGGG LVQPGGSLRL SCAASGFTFD ISAMSWVRQA PGKGLEWVST ISGSAYSTYY 60
ADSVKGRFTI SRDNSKSTLY LQMNSLRAED TAVYYCAREI FSDYWGGLTGL VTVSSASTKG 120
PSVFLAPCS RSTSESTAAL GCLVKDYFPE PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL 180
SSVVTVPSS LGTKTYTCNV DHKPSNTKVD KRVESKYGPP CPPCPAPEFA GAPSFLFPP 240
KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NWYVDGVEVH NAKTKPREEQ FNSTYRVVSV 300
LTVLHQDWLN GKEYKCKVSN KGLPSSIEKT ISKAKGQPRE PQVYTLPPSQ EEMTKNQVSL 360
TCLVKGFYPS DIAVEWESNG QPENNYKTTT PVLDSGGSFF LYSRLTVDKS RWQEGNVFSC 420
SVMHEALHNN YTQKSLSLSL GKAPASSSTK KTQLQLEHLL LALQMILNGI NNYKNPKLTE 480
MLTFKFMYPK KATELKHLC LEEELKPLEE VLNLAQSKNF HLRPRDLISN INVIVLELKG 540
SETTFMCEYA DETATIVEFL NRWITFAQSI ISTLT 575

```

```

SEQ ID NO: 558      moltype = AA length = 575
FEATURE           Location/Qualifiers
source            1..575
                  mol_type = protein
                  organism = Synthetic construct

```

```

SEQUENCE: 558
DVQLVESGGG LVQPGGSLRL SCAASGFTFD ISAMSWVRQA PGKGLEWVST ISGSAYSTYY 60

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-continued

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ADSVKGRPTI SRDNSKSTLY LQMNSLRAED TAVYYCAREI FSDYWGLGTL VTVSSASTKG 120
PSVFPPLAPCS RSTSESTAAL GCLVKDYFPE PVTVSWNSGA LTSGVHTFPA VLQSSGLYSL 180
SSVVTVPSSS LGTKTYTCNV DHKPSNTKVD KRVESKYGPP CPPCPAPEFE GGPSVFLFPP 240
KPKDTLMISR TPEVTCVVVD VSQEDPEVQF NQYVDGVEVH NAKTKPREEQ FNSTYRVVSV 300
LTVLHQDWLN GKEYKCKVSN KGLGSSIEKT ISKAKGQPRE PQVYTLPPSQ EEMTKNQVSL 360
TCLVKGFYPS DIAVEWESNG QPENNYKTPP PVLDSGDSFF LYSRLTVDKS RWQEGNVFSC 420
SVMHEALHMH YTQKSLSLSL GKAPASSSTK KTQLQLEHLL LALQMLNGI NNYKNPKLTE 480
MLTFKFPYMPK KATELKHLCQ LBEELKPLEE VLNLAQSKNF HLRPRDLISN INVIVLELKG 540
SETTFMCEYA DETATIVEFL NRWITFAQSI ISTLT 575

```

```

SEQ ID NO: 559      moltype = AA length = 439
FEATURE            Location/Qualifiers
source             1..439
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 559
QVQLVESGGG VVQPGRSLRL DCKASGITFS NSGMHWVRQA PGKGLEWVAV IWYDGSKRY 60
ADSVKGRPTI SRDNSKNTLF LQMNSLRAED TAVYYCATND DYWGQGLT VSSASTKGPS 120
VFPLAPCSRS TSESTAALGC LVKDYFPEPV TVSWNSGALT SGVHTFPAVL QSSGLYSLSS 180
VVTVPSSSLG TKTYTCNVHD KPSNTKVDKR VESKYGPPCP PCPAPEFLGG PSVFLFPPKP 240
KDTLMISRTPEVTCVVVDV QEDPEVQFNW YVDGVEVHNA KTKPREEQFN STYRVVSVLT 300
VLHQDWLNGK EYKCKVSNKG LPSSIEKTIK KAKGQPREPQ VYTLPPSQEE MTKNQVSLTC 360
LVKGFYPSDI AVEWESNGQP ENNYKTPPVV LDSDGSPFLY SRLTVDKSRW QEGNVFSCSV 420
MHEALHMHYT QKSLSLSLG 439

```

```

SEQ ID NO: 560      moltype = AA length = 451
FEATURE            Location/Qualifiers
source             1..451
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 560
QVQLQQPGAE LVKPGASVKM SCKASGYTFT SYNMHVVKQT PGRGLEWIGA IYPGNGDTSY 60
NQKFKGKATL TADKSSSTAY MQLSSLTSED SAVYYCARST YGGDWYFNV WGAGTIVTVS 120
AASTKGPSVF PLAPSSKSTS GGTAALGCLV KDYFPEPVTV SWNSGALTSG VHTFPAVLQS 180
SGLYSLSSVV TVPSSSLGTQ TYICNVNHPK SNTKVDKKEV PKSCDKTHTC PPCPAPELLG 240
GPSVFLFPPK PKDTLMISRT PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY 300
NSTYRVVSVL TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD 360
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTPPVV LDSDGSPFLY YSKLTVDKSR 420
WQQGNVFSQS VMHEALHMHY TQKSLSLSPG K 451

```

```

SEQ ID NO: 561      moltype = AA length = 450
FEATURE            Location/Qualifiers
source             1..450
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 561
QVQLQQPGAE LVKPGASVKM SCKASGYTFT SYNMHVVKQT PGRGLEWIGA IYPGNGDTSY 60
NQKFKGKATL TADKSSSTAY MQLSSLTSED SAVYYCARST YGGDWYFNV WGAGTIVTVS 120
AASTKGPSVF PLAPSSKSTS GGTAALGCLV KDYFPEPVTV SWNSGALTSG VHTFPAVLQS 180
SGLYSLSSVV TVPSSSLGTQ TYICNVNHPK SNTKVDKKEV PKSCDKTHTC PPCPAPELLG 240
APSVFLFPPK PKDTLMISRT PEVTCVVVDV SHEDPEVKFN WYVDGVEVHN AKTKPREEQY 300
NSTYRVVSVL TVLHQDWLNG KEYKCKVSNK ALPAPIEKTI SKAKGQPREP QVYTLPPSRD 360
ELTKNQVSLT CLVKGFYPSD IAVEWESNGQ PENNYKTPPVV LDSDGSPFLY YSKLTVDKSR 420
WQQGNVFSQS VMHEALHMHY TQKSLSLSPG 450

```

```

SEQ ID NO: 562      moltype = AA length = 213
FEATURE            Location/Qualifiers
source             1..213
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 562
QIVLSQSPAI LSASPGEKVT MTCRASSSVS YIHWFQQKPG SSPKPWIYAT SNLASGVVPR 60
FSGSGSGTSY SLTISRVEAE DAATYYCQQW TSNPPTFGGG TKLEIKRTVA APSVFIFPPS 120
DEQLKSGTAS VVCLLNNFYF REAKVQWKVD NALQSGNSQE SVTBQDSKDS TYSLSLTLTL 180
SKADYEKHKV YACEVTHQGL SSPVTKSPNR GEC 213

```

```

SEQ ID NO: 563      moltype = AA length = 580
FEATURE            Location/Qualifiers
source             1..580
                   mol_type = protein
                   organism = Synthetic construct

```

```

SEQUENCE: 563
EVQLVESGGG LVQPGRSLKL SCAVSGFTFS DYAMAWVRQA PKKGLEWVAT ISYDGSRTYY 60
RDSVKGRPTI SRDNAKITLY LQMDLSLSED TATYYCARHG SGYFDYWGQG VMVTVSSAST 120
KGPSVFPLAP SSKSTSGGTA ALGCLVKDYF PEPVTVSWNS GALTSGVHTF PAVLQSSGLY 180
SLSSVVTVPS SSLGTQYIIC NVNHPKPSNTK VDKKVEPKSC DKHTCTPCPP APFLAGAPSV 240
FLFPPKPKDT LMISRTPEVT CVVVDVSHED PEVKFNWYVD GVEVHNAKTK PREEQYNSTY 300
RVVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTIKAK GQPREPQVYT LPPSRDELTK 360
NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTTPVLDS DGSFPLYSKL TVDKSRWQQG 420

```

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| | | | | | | |
|------------|------------|------------|------------|------------|------------|-----|
| NVFCSCVMHE | ALHNHYTQKS | LSLSPGKAPA | SSSTKKTQLQ | LEHLLLDLQM | ILNGINNYKN | 480 |
| PKLTRMLTFK | FYMPKKATEL | KHLQCLEEEL | KPLEEVLNLA | QSKNFHLRPR | DLISINIVIV | 540 |
| LELKGSETTF | MCEYADETAT | IVEFLNRWIT | FAQSIISTLT | | | 580 |

SEQ ID NO: 564 moltype = AA length = 456
 FEATURE Location/Qualifiers
 source 1..456
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 564

| | | | | | | |
|------------|------------|------------|-------------|------------|------------|-----|
| EVQLQESGPG | LVKPSQSLSL | TCSVTGYSIT | SSYRWNWIRK | FPGNRLEWVG | YINSAGISNY | 60 |
| NPSLKRRIIS | TRDTSKNQFF | LQVNSVTTED | AATYYCARSD | NMGTPPPTYW | GQGTLVTVSS | 120 |
| AKTTPPSVYP | LAPGCGDTTG | SSVTLGCLVK | GYFPESVTVT | WNSGSLSSSV | HTFPALLQSG | 180 |
| LYTMSSSVTV | PSSTWPSQTV | TCSVAHPASS | TTVDKKELEPS | GPISTINPCP | PCKECHKCPA | 240 |
| PNLEGGPSVF | IFPPNIKDVL | MISLTPKVTG | VVDVSEDDP | DVQISWVFN | VEVHTAQQT | 300 |
| HREDYASTIR | VVSTLPIQHQ | DWMSGKEFKC | KVNNDLPSP | IERTISKIKG | LVRAPQVYIL | 360 |
| PPPAEQLSRK | DVSLTCLVVG | FNPGDISVEW | TSNGHTEENY | KDTAPVLDS | GSYFIYSKLN | 420 |
| MKTSKWEKTD | SFSCNVRHEG | LKNYYLKKTI | SRSPGK | | | 456 |

SEQ ID NO: 565 moltype = AA length = 595
 FEATURE Location/Qualifiers
 source 1..595
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 565

| | | | | | | |
|------------|------------|------------|-------------|------------|------------|-----|
| EVQLQESGPG | LVKPSQSLSL | TCSVTGYSIT | SSYRWNWIRK | FPGNRLEWVG | YINSAGISNY | 60 |
| NPSLKRRIIS | TRDTSKNQFF | LQVNSVTTED | AATYYCARSD | NMGTPPPTYW | GQGTLVTVSS | 120 |
| AKTTPPSVYP | LAPGCGDTTG | SSVTLGCLVK | GYFPESVTVT | WNSGSLSSSV | HTFPALLQSG | 180 |
| LYTMSSSVTV | PSSTWPSQTV | TCSVAHPASS | TTVDKKELEPS | GPISTINPCP | PCKECHKCPA | 240 |
| PNLEGGPSVF | IFPPNIKDVL | MISLTPKVTG | VVDVSEDDP | DVQISWVFN | VEVHTAQQT | 300 |
| HREDYASTIR | VVSTLPIQHQ | DWMSGKEFKC | KVNNDLPSP | IERTISKIKG | LVRAPQVYIL | 360 |
| PPPAEQLSRK | DVSLTCLVVG | FNPGDISVEW | TSNGHTEENY | KDTAPVLDS | GSYFIYSKLN | 420 |
| MKTSKWEKTD | SFSCNVRHEG | LKNYYLKKTI | SRSPGSGG | GSAPTSSSTK | KTQLQLEHLL | 480 |
| LDLQMLLNGI | NNYKNPKLTR | MLTKKFRMPK | KATELKHLC | LEBELKPLEE | RLNLAQSKNF | 540 |
| HLRPRDLISN | INVIVLELKG | SETTFMCEYA | DETATIVEFL | NRWITFCQSI | ISTLT | 595 |

SEQ ID NO: 566 moltype = AA length = 218
 FEATURE Location/Qualifiers
 source 1..218
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 566

| | | | | | | |
|------------|------------|------------|------------|------------|------------|-----|
| DIVMTQGTLP | NPVPSGESVS | ITCRSSKSL | YSDGKTYLNV | YLQRPQSQ | LLIYWMSTRA | 60 |
| SGVSDRFSGS | GSQDFTLKI | SGVEADVGI | YQCQGLEFP | TFGGGKLEL | KRADAAPTVS | 120 |
| IFPPSSEQLT | SGGASVVCFL | NNFYPKDIN | KWKIDGSEFQ | NGVLNSWTDQ | DSKDSYSTMS | 180 |
| STLTLTKDEY | ERHNSYTCEA | THKTSTSPIV | KSFNRNEC | | | 218 |

SEQ ID NO: 567 moltype = AA length = 455
 FEATURE Location/Qualifiers
 source 1..455
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 567

| | | | | | | |
|------------|------------|------------|------------|------------|------------|-----|
| EVQLVESGGG | LVQPGRSLKL | SCAASGFTFG | DYSMAWVRQA | PKRGLEWVAN | IIYDGSRTFY | 60 |
| RDSVKGRFTI | SRDNAKPTLY | LQMDSLRPED | TATYYCATHN | YPGYAMEAWG | QGTSTVSSA | 120 |
| KTPPSVYPL | APGCGDTTGS | SVTLGCLVK | YFPESVTVW | NSGSLSSSVH | TFPALLQSG | 180 |
| YTMSSSVTV | SSTWPSQTV | CSVAHPASST | TVDKKLEPSG | PISTINPCPP | CCKECHKCPA | 240 |
| NLEGGPSVFI | FPPNIKDVL | ISLTPKVTG | VVDVSEDDP | VQISWVFN | EVHTAQQT | 300 |
| REDYASTIRV | VSTLPIQHQ | WMSGKEFKCK | VNNDLPSP | ERTISKIKGL | VRAQVYIILP | 360 |
| PPAEQLSRKD | VSLTCLVVG | NPGDISVEW | SNGHTEENY | DTAPVLDS | SYFIYSKLN | 420 |
| KTSKWEKTD | FSCNVRHEGL | KNYYLKKTI | RSPGK | | | 455 |

SEQ ID NO: 568 moltype = AA length = 213
 FEATURE Location/Qualifiers
 source 1..213
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 568

| | | | | | | |
|------------|-------------|------------|------------|------------|------------|-----|
| DTVLTQSPAL | PVSLGQVRNI | SCRATKSVSR | YVHWYQKSG | QQPRLLIYTT | SNLESGVPSR | 60 |
| FSGSGSGTDF | TLTIDPVEAD | DIANYYCQQS | NEIPYTFGAG | TKLELRKADA | APTVSIFPPS | 120 |
| SEQLTSGGAS | VVCFLLNFFYP | KDINVKWKID | GSERQNGVLN | SWTDQDSKDS | TYSMSSTLTL | 180 |
| TKDEYERHNS | YTCEATHKTS | TSPIVKSFN | NEC | | | 213 |

SEQ ID NO: 569 moltype = AA length = 594
 FEATURE Location/Qualifiers
 source 1..594
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 569

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EVQLVESGGG LVQPGRSLKL SCAASGFTFG DYMAWVRQA PKRGLEWVAN IYDGSRTFY 60
RDSVKGRFTI SRDNAKPTLY LQMDSLRPED TATYYCATHN YPGYAMEAWG QGTSVTVSSA 120
KTTTPSVYPL APGCGDPTGS SVTLGCLVKG YFPESVTVTW NSGSLSSSVH TFPALLQSG 180
YTMSSSVTVF SSTWPSQTVT CSAVHPASST TVDKKLEPSG PISTINPCPP CKECHKCPAP 240
NLEGGPSVFP FPPNIKDVLM ISLTPKVTCV VVDVSEDDPD VQISWVFNV EVHTAQQTQTH 300
REDYASTIRV VSTLPIQHGD WMSGKEFKCK VNNKDLPSPI ERTISKIKGL VRAPQVYILP 360
PPAEQLSRKD VSLTCLVGF NPGDISVEWT SNGHTEENYK DTAPVLSDG SYFIYKLNLM 420
KTSKWEKTDS FSCNVRHEGL KNYLKKTTIS RSPGKSGGGG SAPTSSSTKK TQLQLEHLLL 480
DLQMILNGIN NYKNPKLTRM LTKKFRMPK ATELKHLQCL EEBELKPLEER LNLAQSKNFH 540
LRPRDLISNI NVIVLELKG ETTFMCEYAD ETATIVEEFLN RWITFCQSI STLT 594

```

```

SEQ ID NO: 570      moltype = AA length = 595
FEATURE           Location/Qualifiers
source            1..595
                  mol_type = protein
                  organism = Synthetic construct

```

```

SEQUENCE: 570
EVQLVGGGGG LVQPGGSLKL SCAASGFTFS DFYMAWVRQA PTKGLEWVAS ISTGGGNTHY 60
RDSVKGRFTI SRDNAKSTLY LQMDSLRSEE TATYYCARLL STISTPPDYW GQGVIVTVSS 120
AKTTPPSVYP LAPGCGDTTG SSVTLGCLVK GYFPESVTVT WNSGSLSSSV HTFPALLQSG 180
LYTMSSSVTV PSSTWPSQTV TCSVAHPASS TVVDKLEPS GPISITINPCP PCKECKKCPA 240
PNLEGGPSVF IFPPNIKDVLM MISLTPKVTC VVDVSEDDPD DVQISWVFN VEVHTAQQTQ 300
HREDYASTIR VVSTLPIQHGD DWMSGKEFKC KVNKDLPSPI IERTISKIKG LVRAPQVYIL 360
PPPAEQLSRK DVSLTCLVGF FNPDISVEW TSNHTEENY KDTAPVLSDG GSYFIYKLNLM 420
MKTSKWEKTD SFCNVRHEGL LKNYLLKTTI SRSPGKSGGG GSAPTSSSTK TQLQLEHLLL 480
LDLQMILNGI NNYKNPKLTR MLTKKFRMPK KATELKHLC EEBELKPLEE RNLAQSKNF 540
HLRPRDLISN INVIVLELKG SETTFMCEYA DETATIVEEFL NRWITFCQSI ISTLT 595

```

```

SEQ ID NO: 571      moltype = AA length = 214
FEATURE           Location/Qualifiers
source            1..214
                  mol_type = protein
                  organism = Synthetic construct

```

```

SEQUENCE: 571
DVVLIQSPTT LSVTPGETVS LSCRASHSVG TNLHWYQORT NESPSLLIKY SSHSTSGIPS 60
RFSATGSGTD FTLNISNVEF DDVASYFCQQ SQKWPLTFGS GTKLEIKRAD AAPTIVSIFPP 120
SSEQLTSGGA SVVCFLNIFY PKDINVKWKI DGSERQNGVL NSWTDQDSKD STYSMSSTLT 180
LTKDEYERHN SYTCEATHKT STSPIVKSFN RNEC 214

```

```

SEQ ID NO: 572      moltype = AA length = 591
FEATURE           Location/Qualifiers
source            1..591
                  mol_type = protein
                  organism = Synthetic construct

```

```

SEQUENCE: 572
EVQLQQSGPE LVKPGASVKI SCKTSGYTFT EYTMHWVKQS HGKSLEWIGG INPNNGTTY 60
NQKFKGKATL TVDKSSSTAY MELRSLTSQD SAVYYCARDY YRYGHYYAMD YWQGTSTVTV 120
SSASTKGPSV FPLAPSSKST SGGTAAALGCL VKDYFPPEPVT VSWNSGALTS GVHTFPAPVLQ 180
SSGLYSLSSV VTPSSSLGT QTYICNVNHHK PSNTKVDKKV EPKSCDKTHT CPPCPAPELL 240
GGPSVFLFPP KPKDTLMISR TPEVTCVVVD VSHEDPEVKF NWYVDGVEVH NAKTKPREEQ 300
YNSYRVRVSV LTVLHQDWLNL GKEYKCKVSN KALPAPIEKT ISKAKGQPRE PQVYITLPPSR 360
DELTKNQVSL TCLVKGFYPS DIAVEWESNG QPENNYKTFP VLDSGDSGFF LYSKLTVDKS 420
RWQQGNVFCF SVMHEALHNN YTKSLSLSP GKSGGGGSAP TSSSTKKTQL QLEHLLLDLQ 480
MILNGINNYK NPKLTRMLTF KFYMPKKATE LKHLQCLEEE LKPLEEVLNL AQSKNFHLRP 540
RDLISNINVI VLELKGSETT FMCEYADETA TIVEFLNRWI TFCQSIISTL T 591

```

```

SEQ ID NO: 573      moltype = AA length = 213
FEATURE           Location/Qualifiers
source            1..213
                  mol_type = protein
                  organism = Synthetic construct

```

```

SEQUENCE: 573
QIVLTQSPAI MSASPGEKVT MTCVSSSVR FMHWYQQKSG TSPKRWIYDT SKLASGVPAR 60
FSGSGSTSY SLTISSMEAE DAATYYCQQW SSNPPTFGGG TKLKIKRTVA APSVFIKPPS 120
DEQLKSGTAS VVCLLNNFYP REAKVQWKVD NALQSGNSQE SVTEQDSKDS TYSLSSTLTL 180
SKADYEKHKV YACEVTHQGL SSPVTKSFNR GEC 213

```

```

SEQ ID NO: 574      moltype = AA length = 133
FEATURE           Location/Qualifiers
source            1..133
                  mol_type = protein
                  organism = Synthetic construct

```

```

SEQUENCE: 574
APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TAKFAMPKKA TELKHLQCLE 60
EELKPLEEVL NGAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

```

```

SEQ ID NO: 575      moltype = AA length = 133
FEATURE           Location/Qualifiers

```

-continued

```

source                1..133
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 575
APTSSSTKKT QLQLEALLLD LQMILNGINN YKNPKLTRML TAKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT                                     133

SEQ ID NO: 576        moltype = AA length = 448
FEATURE              Location/Qualifiers
source                1..448
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 576
EVQLLESGGG LVQPGGSLRL SCVSGGFNLK DYCMTWVRQA PGKGLEWVSA IVYSGGSTYY 60
ADSVKGRPTI SRDNSKNTLY LQMNSLRAED TAVYYCAKYT RGSYFYDAMD VWGQGTTVTV 120
SSASTKGPSV FPLAPCSRST SESTAALGCL VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ 180
SSGLYSLSSV VTPSSSLGT KTYTCNVDPK PSNTKVDKRV ESKYGPCCPP CPAPEPLGGP 240
SVFLFPPKPK DTLMISRPE VTCVVVDVSG EDPEVQFNWY VDGVEVHNAK TKPREEQFNS 300
TYRVVSVLTV LHQDNLNGKE YKCKVSNKGL PSSIEKTISK AKGQPREPQV YTLPPSQEEM 360
TKNQVSLTCL VKGFYPSDIA VEWESNGQPE NNYKTPPVLD DSDGSFFLYS RLTVDKSRWQ 420
EGNVFSCSVM HEALHNHYTQ KSLSLSLG                                     448

SEQ ID NO: 577        moltype = AA length = 448
FEATURE              Location/Qualifiers
source                1..448
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 577
EVQLLESGGG LVQPGGSLRL SCVSGGFNFK DYCMTWVRQA PGKGLEWVSA IVYSGGSTYY 60
ADSVKGRPTI SRDNSKNTLY LQMNSLRAED TAVYYCAKYT RGSYFYDAMD VWGQGTTVTV 120
SSASTKGPSV FPLAPCSRST SESTAALGCL VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ 180
SSGLYSLSSV VTPSSSLGT KTYTCNVDPK PSNTKVDKRV ESKYGPCCPP CPAPEPLGGP 240
SVFLFPPKPK DTLMISRPE VTCVVVDVSG EDPEVQFNWY VDGVEVHNAK TKPREEQFNS 300
TYRVVSVLTV LHQDNLNGKE YKCKVSNKGL PSSIEKTISK AKGQPREPQV YTLPPSQEEM 360
TKNQVSLTCL VKGFYPSDIA VEWESNGQPE NNYKTPPVLD DSDGSFFLYS RLTVDKSRWQ 420
EGNVFSCSVM HEALHNHYTQ KSLSLSLG                                     448

SEQ ID NO: 578        moltype = AA length = 446
FEATURE              Location/Qualifiers
source                1..446
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 578
QVQLVQSGVE VKKPGASVKV SCKASGYTFT NYYMYWVRQA PGQGLEWVSA INPSNGGTNF 60
NEKFKNRVTL TTDSTTTAY MELKSLQFDD TAVYYCARRD YRFDMGFDYW GQGTTVTVSS 120
ASTKGPSVFP LAPCSRSTSE STAALGCLVK DYFPEPVTVS WNSGALTSV HTFPAVLQSS 180
GLYSLSSVVT VPSSSLGTKT YTCNVDPKPS NTKVDKRVES KYGPPCCPPCP APEFLGGPSV 240
FLFPPKPKDT LMI SRTP EVT CVVVDVSDQ EDPEVQFNWYVD GVEVHNAKTK PREEQFNSTY 300
RVVSVLTVLH QDNLNGKEYK CKVSNKGLPS SIEKTISKAK GQPREPQVYT LPPSQEEMTK 360
NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTPPVLDSD DGSFFLYSRL TVDKSRWQEG 420
NVFSCSVMHE ALHNHYTQKS LSLSLG                                     446

SEQ ID NO: 579        moltype = AA length = 218
FEATURE              Location/Qualifiers
source                1..218
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 579
EIVLTQSPAT LSLSPGERAT LSCRASKGVS TSGYSYLHWY QQKPGQAPRL LIYLASYLES 60
GVPARFSGSG SGTDFLTITIS SLEPEDFAVY YCQHSRDLPL TFGGKTKVEI KRTVAAPSVF 120
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| RDSVKGRFTI SRDNAKSTLY | LQMDLSRSEE TATYYCARLL | STISTPPDYW GQGVIVTVSS | 120 |
| ASTKGPSVFP LAPCSRSTSE | STAALGCLVK DYFPEPVTVS | WNSGALTSKV HTFPAVLQSS | 180 |
| GLYSLSSVVT VPSSSLGTKT | YTCNVDPKPS NTKVDKRVES | KYGPCCPPCP APEFLGGPSV | 240 |
| FLFPPKPKDT LMIKRTPEVT | CVVVDVQSED PEVQFNWYVD | GVEVHNAKTK PREEQFNSTY | 300 |
| RVSVLTIVLH QDWLNGKEYK | CKVSNKGLPS SIEKTIKAK | GQPREPQVYT LPPSQEEMTK | 360 |
| NQVSLTCLVK GFYPSDIAVE | WESNGQPENN YKTTTPVLDL | DGSFFLYSRL TVDKSRWQEG | 420 |
| NVDFCSVMHE ALHNHYTQKS | LSLSLGLK | | 447 |
| SEQ ID NO: 586 | moltype = AA length = 214 | | |
| FEATURE | Location/Qualifiers | | |
| source | 1..214 | | |
| | mol_type = protein | | |
| | organism = Synthetic construct | | |
| SEQUENCE: 586 | | | |
| DVVLIQSPPT LSVTPGETVS | LSCRASHSVG TNLHWYQQRT | NESPSLLIKY SSHSTSGIPS | 60 |
| RFSATGSGTD FTLNISNVEF | DDVASYFCQQ SQKWPLTFGS | GTKLEIKRTV AAPSVFIFPP | 120 |
| SDEQLKSGTA SVVCLLNIFY | PREAKVQWKV DNALQSGNSQ | ESVTEQDSKD STYSLSTLT | 180 |
| LSKADYEKHK VYACEVTHQG | LSSPVTKSFN RQEC | | 214 |
| SEQ ID NO: 587 | moltype = AA length = 770 | | |
| FEATURE | Location/Qualifiers | | |
| source | 1..770 | | |
| | mol_type = protein | | |

-continued

organism = Synthetic construct

SEQUENCE: 587

| | | | | | | |
|-------------|------------|------------|------------|------------|------------|-----|
| EVQLVESGGG | LVQPGRSLKL | SCAVSGFTFS | DYAMAWVRQA | PKKGLEWVAT | ISYDGSRTYY | 60 |
| RDSVKGRFTI | SRDNAKITLY | LQMDSLRSED | TATYYCARHG | SGYFDYWQGG | VMVTVSSAST | 120 |
| KGPSVFPPLAP | SSKSTSGGTA | ALGCLVKDYF | PEPVTVSWNS | GALTSGVHTF | PAVLQSSGLY | 180 |
| SLSSVVTVPS | SSLGTQTYIC | NVNHKPSNTK | VDKKVEPKSC | DKTHTCPPCP | APELLGGPSV | 240 |
| FLFPPKPKD | LMISRTPEVT | CVVVDVSHED | PEVKFNWYVD | GVEVHNAKTK | PREEQYNSTY | 300 |
| RVSVLTVLH | QDWLNGKEYK | CKVSNKALPA | PIEKTISKAK | GQPREPQVYT | LPPSRDELTK | 360 |
| NQVSLTCLVK | GFYPSDIAVE | WESNGQPENN | YKTTTPVLDS | DGSFFLYSKL | TVDKSRWQQG | 420 |
| NVFCSCVMHE | ALHNHYTQKS | LSLSPGKSGG | GGSELCDDDP | PEIPHATFKA | MAYKEGTMNL | 480 |
| CECKRGRFRI | KSGSLYMLCT | GNSHSSWDN | QCQCTSSATR | NTTKQVTPQP | EEQKERKTE | 540 |
| MQSPMQPVDQ | ASLPGHCREP | PPWENEATER | IYHFVVGQMV | YYQCVQGYRA | LHRGPAESVC | 600 |
| KMTHGKTRWT | QPQLICTSGG | GGSGGGSGG | GGSGGGSAPT | SSSTKKTQLQ | LAHLLLDLQM | 660 |
| ILNGINNYKN | PKLTRLMTFK | FYMPKKATEL | KHLQCLEEEL | KPLEEVLNLA | QSKNFHLRPR | 720 |
| DLISINIVIV | LELKGSETTF | MCEYADETAT | IVEFLNRWIT | FCQSIISTLT | | 770 |

SEQ ID NO: 588 moltype = AA length = 770
 FEATURE Location/Qualifiers
 source 1..770
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 588

| | | | | | | |
|-------------|------------|------------|------------|------------|------------|-----|
| EVQLVESGGG | LVQPGRSLKL | SCAVSGFTFS | DYAMAWVRQA | PKKGLEWVAT | ISYDGSRTYY | 60 |
| RDSVKGRFTI | SRDNAKITLY | LQMDSLRSED | TATYYCARHG | SGYFDYWQGG | VMVTVSSAST | 120 |
| KGPSVFPPLAP | SSKSTSGGTA | ALGCLVKDYF | PEPVTVSWNS | GALTSGVHTF | PAVLQSSGLY | 180 |
| SLSSVVTVPS | SSLGTQTYIC | NVNHKPSNTK | VDKKVEPKSC | DKTHTCPPCP | APELLGGPSV | 240 |
| FLFPPKPKD | LMISRTPEVT | CVVVDVSHED | PEVKFNWYVD | GVEVHNAKTK | PREEQYNSTY | 300 |
| RVSVLTVLH | QDWLNGKEYK | CKVSNKALPA | PIEKTISKAK | GQPREPQVYT | LPPSRDELTK | 360 |
| NQVSLTCLVK | GFYPSDIAVE | WESNGQPENN | YKTTTPVLDS | DGSFFLYSKL | TVDKSRWQQG | 420 |
| NVFCSCVMHE | ALHNHYTQKS | LSLSPGKSGG | GGSELCDDDP | PEIPHATFKA | MAYKEGTMNL | 480 |
| CECKRGRFRI | KSGSLYMLCT | GNSHSSWDN | QCQCTSSATR | NTTKQVTPQP | EEQKERKTE | 540 |
| MQSPMQPVDQ | ASLPGHCREP | PPWENEATER | IYHFVVGQMV | YYQCVQGYRA | LHRGPAESVC | 600 |
| KMTHGKTRWT | QPQLICTSGG | GGSGGGSGG | GGSGGGSAPT | SSSTKKTQLQ | LEHLLLDLQM | 660 |
| ILNGINNYKN | PKLTRLMTFK | FYMPKKATEL | KHLQCLEEEL | KPLEEVLNLA | QSKNFHLRPR | 720 |
| DLISINIVIV | LELKGSETTF | MCEYADETAT | IVEFLNRWIT | FCQSIISTLT | | 770 |

SEQ ID NO: 589 moltype = AA length = 770
 FEATURE Location/Qualifiers
 source 1..770
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 589

| | | | | | | |
|-------------|------------|------------|------------|------------|------------|-----|
| EVQLVESGGG | LVQPGRSLKL | SCAVSGFTFS | DYAMAWVRQA | PKKGLEWVAT | ISYDGSRTYY | 60 |
| RDSVKGRFTI | SRDNAKITLY | LQMDSLRSED | TATYYCARHG | SGYFDYWQGG | VMVTVSSAST | 120 |
| KGPSVFPPLAP | SSKSTSGGTA | ALGCLVKDYF | PEPVTVSWNS | GALTSGVHTF | PAVLQSSGLY | 180 |
| SLSSVVTVPS | SSLGTQTYIC | NVNHKPSNTK | VDKKVEPKSC | DKTHTCPPCP | APELLGGPSV | 240 |
| FLFPPKPKD | LMISRTPEVT | CVVVDVSHED | PEVKFNWYVD | GVEVHNAKTK | PREEQYNSTY | 300 |
| RVSVLTVLH | QDWLNGKEYK | CKVSNKALPA | PIEKTISKAK | GQPREPQVYT | LPPSRDELTK | 360 |
| NQVSLTCLVK | GFYPSDIAVE | WESNGQPENN | YKTTTPVLDS | DGSFFLYSKL | TVDKSRWQQG | 420 |
| NVFCSCVMHE | ALHNHYTQKS | LSLSPGKSGG | GGSELCDDDP | PEIPHATFKA | MAYKEGTMNL | 480 |
| CECKRGRFRI | KSGSLYMLCT | GNSHSSWDN | QCQCTSSATR | NTTKQVTPQP | EEQKERKTE | 540 |
| MQSPMQPVDQ | ASLPGHCREP | PPWENEATER | IYHFVVGQMV | YYQCVQGYRA | LHRGPAESVC | 600 |
| KMTHGKTRWT | QPQLICTSGG | GGSGGGSGG | GGSGGGSAPT | SSSTKKTQLQ | LEHLLLDLQM | 660 |
| ILNGINNYKN | PKLTRLMTFK | FYMPKKATEL | KHLQCLEEEL | KPLEEVLNLA | QSKNFHLRPR | 720 |
| DLISINIVIV | LELKGSETTF | MCEYADETAT | IVEFLNRWIT | FCQSIISTLT | | 770 |

SEQ ID NO: 590 moltype = AA length = 770
 FEATURE Location/Qualifiers
 source 1..770
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 590

| | | | | | | |
|-------------|------------|------------|------------|------------|------------|-----|
| EVQLVESGGG | LVQPGRSLKL | SCAVSGFTFS | DYAMAWVRQA | PKKGLEWVAT | ISYDGSRTYY | 60 |
| RDSVKGRFTI | SRDNAKITLY | LQMDSLRSED | TATYYCARHG | SGYFDYWQGG | VMVTVSSAST | 120 |
| KGPSVFPPLAP | SSKSTSGGTA | ALGCLVKDYF | PEPVTVSWNS | GALTSGVHTF | PAVLQSSGLY | 180 |
| SLSSVVTVPS | SSLGTQTYIC | NVNHKPSNTK | VDKKVEPKSC | DKTHTCPPCP | APELLGGPSV | 240 |
| FLFPPKPKD | LMISRTPEVT | CVVVDVSHED | PEVKFNWYVD | GVEVHNAKTK | PREEQYNSTY | 300 |
| RVSVLTVLH | QDWLNGKEYK | CKVSNKALPA | PIEKTISKAK | GQPREPQVYT | LPPSRDELTK | 360 |
| NQVSLTCLVK | GFYPSDIAVE | WESNGQPENN | YKTTTPVLDS | DGSFFLYSKL | TVDKSRWQQG | 420 |
| NVFCSCVMHE | ALHNHYTQKS | LSLSPGKSGG | GGSELCDDDP | PEIPHATFKA | MAYKEGTMNL | 480 |
| CECKRGRFRI | KSGSLYMLCT | GNSHSSWDN | QCQCTSSATR | NTTKQVTPQP | EEQKERKTE | 540 |
| MQSPMQPVDQ | ASLPGHCREP | PPWENEATER | IYHFVVGQMV | YYQCVQGYRA | LHRGPAESVC | 600 |
| KMTHGKTRWT | QPQLICTSGG | GGSGGGSGG | GGSGGGSAPT | SSSTKKTQLQ | LEHLLLDLQM | 660 |
| ILNGINNYKN | PKLTRLMTFK | FYMPKKATEL | KHLQCLEEEL | KPLEEVLNLA | QSKNFHLRPR | 720 |
| DLISINIVIV | LELKGSETTF | MCEYADETAT | IVEFLNRWIT | FCQSIISTLT | | 770 |

SEQ ID NO: 591 moltype = AA length = 770
 FEATURE Location/Qualifiers
 source 1..770

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mol_type = protein
organism = Synthetic construct

SEQUENCE: 591
EVQLVESGGG LVQPGRSLKL SCAVSGFTFS DYAMAWVRQA PPKGLEWVAT ISYDGSRTYY 60
RDSVKGRFTI SRDNAKITLY LQMDSLRSSE TATYYCARHG SGYFDYWQGG VMVTVSSAST 120
KGPSVFPLAP SSKSTSGGTA ALGCLVKDYF PEPVTVSWNS GALTSQVHTF PAVLQSSGLY 180
SLSSVVTVPS SSLGTQTYIC NVNHKPSNTK VDKKVEPKSC DKHTHTCPPCP APELLGGPSV 240
FLFPPKPKDT LMI SRTPEVT CVVVDVSHED PEVKFNWYVD GVEVHNAKTK PREEQYNSTY 300
RVVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK GQPREPQVYT LPPSRDELTK 360
NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTTPVLDS DGSFFLYSKL TVDKSRWQQG 420
NVFSCSVME ALHNHYTQKS LSLSPGKSGG GGSELCDDDP PEIPHATFKA MAYKEGTMNL 480
CECKRGRFRI KSGSLYMLCT GNSHSSWDN QCQCTSSATR NTKQVTPQP EEQKERKTE 540
MQSPMQPVDQ ASLPGHCREP PPWENEATER IYHFVVGQMV YYQCVQGYRA LHRGPAESVC 600
KMTGKTRWT QPQLICTSGG GSGGGGSGG GSGGGGSAPT SSSTKKTQLQ LEHLLWLQM 660
ILNGINNYKN PKLTRMLTFK FYMPKKATEL KHLQCLEEEL KPLBEVLNLA QSKNFHLRPR 720
DLISNINIV LELKGSSETF MCEYADETAT IVEFLNRWIT FCQSIISTLT 770

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SEQ ID NO: 592      moltype = AA length = 770
FEATURE           Location/Qualifiers
source           1..770
                 mol_type = protein
                 organism = Synthetic construct

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SEQUENCE: 592
EVQLVESGGG LVQPGRSLKL SCAVSGFTFS DYAMAWVRQA PPKGLEWVAT ISYDGSRTYY 60
RDSVKGRFTI SRDNAKITLY LQMDSLRSSE TATYYCARHG SGYFDYWQGG VMVTVSSAST 120
KGPSVFPLAP SSKSTSGGTA ALGCLVKDYF PEPVTVSWNS GALTSQVHTF PAVLQSSGLY 180
SLSSVVTVPS SSLGTQTYIC NVNHKPSNTK VDKKVEPKSC DKHTHTCPPCP APELLGGPSV 240
FLFPPKPKDT LMI SRTPEVT CVVVDVSHED PEVKFNWYVD GVEVHNAKTK PREEQYNSTY 300
RVVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK GQPREPQVYT LPPSRDELTK 360
NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTTPVLDS DGSFFLYSKL TVDKSRWQQG 420
NVFSCSVME ALHNHYTQKS LSLSPGKSGG GGSELCDDDP PEIPHATFKA MAYKEGTMNL 480
CECKRGRFRI KSGSLYMLCT GNSHSSWDN QCQCTSSATR NTKQVTPQP EEQKERKTE 540
MQSPMQPVDQ ASLPGHCREP PPWENEATER IYHFVVGQMV YYQCVQGYRA LHRGPAESVC 600
KMTGKTRWT QPQLICTSGG GSGGGGSGG GSGGGGSAPT SSSTKKTQLQ LEHLLLYLQM 660
ILNGINNYKN PKLTRMLTFK FYMPKKATEL KHLQCLEEEL KPLBEVLNLA QSKNFHLRPR 720
DLISNINIV LELKGSSETF MCEYADETAT IVEFLNRWIT FCQSIISTLT 770

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SEQ ID NO: 593      moltype = AA length = 770
FEATURE           Location/Qualifiers
source           1..770
                 mol_type = protein
                 organism = Synthetic construct

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SEQUENCE: 593
EVQLVESGGG LVQPGRSLKL SCAVSGFTFS DYAMAWVRQA PPKGLEWVAT ISYDGSRTYY 60
RDSVKGRFTI SRDNAKITLY LQMDSLRSSE TATYYCARHG SGYFDYWQGG VMVTVSSAST 120
KGPSVFPLAP SSKSTSGGTA ALGCLVKDYF PEPVTVSWNS GALTSQVHTF PAVLQSSGLY 180
SLSSVVTVPS SSLGTQTYIC NVNHKPSNTK VDKKVEPKSC DKHTHTCPPCP APELLGGPSV 240
FLFPPKPKDT LMI SRTPEVT CVVVDVSHED PEVKFNWYVD GVEVHNAKTK PREEQYNSTY 300
RVVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK GQPREPQVYT LPPSRDELTK 360
NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTTPVLDS DGSFFLYSKL TVDKSRWQQG 420
NVFSCSVME ALHNHYTQKS LSLSPGKSGG GGSELCDDDP PEIPHATFKA MAYKEGTMNL 480
CECKRGRFRI KSGSLYMLCT GNSHSSWDN QCQCTSSATR NTKQVTPQP EEQKERKTE 540
MQSPMQPVDQ ASLPGHCREP PPWENEATER IYHFVVGQMV YYQCVQGYRA LHRGPAESVC 600
KMTGKTRWT QPQLICTSGG GSGGGGSGG GSGGGGSAPT SSSTKKTQLQ LEHLLLRQM 660
ILNGINNYKN PKLTRMLTFK FYMPKKATEL KHLQCLEEEL KPLBEVLNLA QSKNFHLRPR 720
DLISNINIV LELKGSSETF MCEYADETAT IVEFLNRWIT FCQSIISTLT 770

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SEQ ID NO: 594      moltype = AA length = 770
FEATURE           Location/Qualifiers
source           1..770
                 mol_type = protein
                 organism = Synthetic construct

```

```

SEQUENCE: 594
EVQLVESGGG LVQPGRSLKL SCAVSGFTFS DYAMAWVRQA PPKGLEWVAT ISYDGSRTYY 60
RDSVKGRFTI SRDNAKITLY LQMDSLRSSE TATYYCARHG SGYFDYWQGG VMVTVSSAST 120
KGPSVFPLAP SSKSTSGGTA ALGCLVKDYF PEPVTVSWNS GALTSQVHTF PAVLQSSGLY 180
SLSSVVTVPS SSLGTQTYIC NVNHKPSNTK VDKKVEPKSC DKHTHTCPPCP APELLGGPSV 240
FLFPPKPKDT LMI SRTPEVT CVVVDVSHED PEVKFNWYVD GVEVHNAKTK PREEQYNSTY 300
RVVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK GQPREPQVYT LPPSRDELTK 360
NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTTPVLDS DGSFFLYSKL TVDKSRWQQG 420
NVFSCSVME ALHNHYTQKS LSLSPGKSGG GGSELCDDDP PEIPHATFKA MAYKEGTMNL 480
CECKRGRFRI KSGSLYMLCT GNSHSSWDN QCQCTSSATR NTKQVTPQP EEQKERKTE 540
MQSPMQPVDQ ASLPGHCREP PPWENEATER IYHFVVGQMV YYQCVQGYRA LHRGPAESVC 600
KMTGKTRWT QPQLICTSGG GSGGGGSGG GSGGGGSAPT SSSTKKTQLQ LEHLLFLQM 660
ILNGINNYKN PKLTRMLTFK FYMPKKATEL KHLQCLEEEL KPLBEVLNLA QSKNFHLRPR 720
DLISNINIV LELKGSSETF MCEYADETAT IVEFLNRWIT FCQSIISTLT 770

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SEQ ID NO: 595      moltype = AA length = 770
FEATURE           Location/Qualifiers

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-continued

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source                1..770
                      mol_type = protein
                      organism = Synthetic construct

SEQUENCE: 595
EVQLVESGGG LVQPGRSLKL SCAVSGFTFS DYAMAWVRQA PPKGLEWVAT ISYDGSRTYY 60
RDSVKGRFTI SRDNAKITLY LQMDLSRSED TATYYCARHG SGYFDYWGQG VMVTVSSAST 120
KGPSVFPPLAP SSKSTSGGTA ALGCLVKDYF PEPVTVSWNS GALTSGVHTF PAVLQSSGLY 180
SLSSVVTVPS SSLGTQTYIC NVNHKPSNTK VDKKVEPKSC DKTHTCPPCP APELLGGPSV 240
FLFPPKPKDPT LMI SRTPEVT CVVVDVSHED PEVKFNWYVD GVEVHNAKTK PREEQYNSTY 300
RVVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK GQPREPQVYV LPPSRDELTK 360
NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTTPVLDS DGSFFLYSKL TVDKSRWQQG 420
NVFSCVMHE ALHNHYTQKS LSLSPGKSGG GGSELCDDDP PEIPHATFKA MAYKEGTM LN 480
CECKRGFRRI KSGSLYMLCT GNSHSSWDN QCQCTSSATR NTTKQVTPQP EEQKERKTE 540
MQSPMQPVDQ ASLPGHCREP PPWENEATER IYHFVVGQMV YYQCVQGYRA LHRGPAESVC 600
KMTHGKTRWT QPQLICTSGG GSGGGGSGG GSGGGGSAPT SSSTKKTQLQ LEHLLLDLQM 660
ILNGINNYKN PKLTRMLTFK FYMPKKATEL KHLQCLEEEL KPLEEVLNLA QSKNFHLRPR 720
KLISNINIV LELKGSSETF MCEYADETAT IVEFLNRWIT FCQSIISTLT 770

```

```

SEQ ID NO: 596        moltype = AA length = 770
FEATURE              Location/Qualifiers
source                1..770
                      mol_type = protein
                      organism = Synthetic construct

```

```

SEQUENCE: 596
EVQLVESGGG LVQPGRSLKL SCAVSGFTFS DYAMAWVRQA PPKGLEWVAT ISYDGSRTYY 60
RDSVKGRFTI SRDNAKITLY LQMDLSRSED TATYYCARHG SGYFDYWGQG VMVTVSSAST 120
KGPSVFPPLAP SSKSTSGGTA ALGCLVKDYF PEPVTVSWNS GALTSGVHTF PAVLQSSGLY 180
SLSSVVTVPS SSLGTQTYIC NVNHKPSNTK VDKKVEPKSC DKTHTCPPCP APELLGGPSV 240
FLFPPKPKDPT LMI SRTPEVT CVVVDVSHED PEVKFNWYVD GVEVHNAKTK PREEQYNSTY 300
RVVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK GQPREPQVYV LPPSRDELTK 360
NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTTPVLDS DGSFFLYSKL TVDKSRWQQG 420
NVFSCVMHE ALHNHYTQKS LSLSPGKSGG GGSELCDDDP PEIPHATFKA MAYKEGTM LN 480
CECKRGFRRI KSGSLYMLCT GNSHSSWDN QCQCTSSATR NTTKQVTPQP EEQKERKTE 540
MQSPMQPVDQ ASLPGHCREP PPWENEATER IYHFVVGQMV YYQCVQGYRA LHRGPAESVC 600
KMTHGKTRWT QPQLICTSGG GSGGGGSGG GSGGGGSAPT SSSTKKTQLQ LEHLLLDLQM 660
ILNGINNYKN PKLTRMLTFK FYMPKKATEL KHLQCLEEEL KPLEEVLNLA QSKNFHLRPR 720
DLIANINIV LELKGSSETF MCEYADETAT IVEFLNRWIT FCQSIISTLT 770

```

```

SEQ ID NO: 597        moltype = AA length = 770
FEATURE              Location/Qualifiers
source                1..770
                      mol_type = protein
                      organism = Synthetic construct

```

```

SEQUENCE: 597
EVQLVESGGG LVQPGRSLKL SCAVSGFTFS DYAMAWVRQA PPKGLEWVAT ISYDGSRTYY 60
RDSVKGRFTI SRDNAKITLY LQMDLSRSED TATYYCARHG SGYFDYWGQG VMVTVSSAST 120
KGPSVFPPLAP SSKSTSGGTA ALGCLVKDYF PEPVTVSWNS GALTSGVHTF PAVLQSSGLY 180
SLSSVVTVPS SSLGTQTYIC NVNHKPSNTK VDKKVEPKSC DKTHTCPPCP APELLGGPSV 240
FLFPPKPKDPT LMI SRTPEVT CVVVDVSHED PEVKFNWYVD GVEVHNAKTK PREEQYNSTY 300
RVVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK GQPREPQVYV LPPSRDELTK 360
NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTTPVLDS DGSFFLYSKL TVDKSRWQQG 420
NVFSCVMHE ALHNHYTQKS LSLSPGKSGG GGSELCDDDP PEIPHATFKA MAYKEGTM LN 480
CECKRGFRRI KSGSLYMLCT GNSHSSWDN QCQCTSSATR NTTKQVTPQP EEQKERKTE 540
MQSPMQPVDQ ASLPGHCREP PPWENEATER IYHFVVGQMV YYQCVQGYRA LHRGPAESVC 600
KMTHGKTRWT QPQLICTSGG GSGGGGSGG GSGGGGSAPT SSSTKKTQLQ LEHLLLDLQM 660
ILNGINNYKN PKLTRMLTFK FYMPKKATEL KHLQCLEEEL KPLEEVLNLA QSKNFHLRPR 720
DLISYINIV LELKGSSETF MCEYADETAT IVEFLNRWIT FCQSIISTLT 770

```

```

SEQ ID NO: 598        moltype = AA length = 770
FEATURE              Location/Qualifiers
source                1..770
                      mol_type = protein
                      organism = Synthetic construct

```

```

SEQUENCE: 598
EVQLVESGGG LVQPGRSLKL SCAVSGFTFS DYAMAWVRQA PPKGLEWVAT ISYDGSRTYY 60
RDSVKGRFTI SRDNAKITLY LQMDLSRSED TATYYCARHG SGYFDYWGQG VMVTVSSAST 120
KGPSVFPPLAP SSKSTSGGTA ALGCLVKDYF PEPVTVSWNS GALTSGVHTF PAVLQSSGLY 180
SLSSVVTVPS SSLGTQTYIC NVNHKPSNTK VDKKVEPKSC DKTHTCPPCP APELLGGPSV 240
FLFPPKPKDPT LMI SRTPEVT CVVVDVSHED PEVKFNWYVD GVEVHNAKTK PREEQYNSTY 300
RVVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK GQPREPQVYV LPPSRDELTK 360
NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTTPVLDS DGSFFLYSKL TVDKSRWQQG 420
NVFSCVMHE ALHNHYTQKS LSLSPGKSGG GGSELCDDDP PEIPHATFKA MAYKEGTM LN 480
CECKRGFRRI KSGSLYMLCT GNSHSSWDN QCQCTSSATR NTTKQVTPQP EEQKERKTE 540
MQSPMQPVDQ ASLPGHCREP PPWENEATER IYHFVVGQMV YYQCVQGYRA LHRGPAESVC 600
KMTHGKTRWT QPQLICTSGG GSGGGGSGG GSGGGGSAPT SSSTKKTQLQ LEHLLLDLQM 660
ILNGINNYKN PKLTRMLTFK FYMPKKATEL KHLQCLEEEL KPLEEVLNLA QSKNFHLRPR 720
DLISDINIV LELKGSSETF MCEYADETAT IVEFLNRWIT FCQSIISTLT 770

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SEQ ID NO: 599        moltype = AA length = 770

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FEATURE                               Location/Qualifiers
source                                1..770
                                        mol_type = protein
                                        organism = Synthetic construct

SEQUENCE: 599
EVQLVESGGG LVQPGRSLKL SCAVSGFTFS DYAMAWVRQA PPKGLEWVAT ISYDGSRTYY 60
RDSVKGRFTI SRDNAKITLY LQMDSLRSER TATYYCARHG SGYPDYWGQG VMVTVSSAST 120
KGPSVFPPLAP SSKSTSGGTA ALGCLVKDYF PEPVTVSWNS GALTSGVHTF PAVLQSSGLY 180
SLSSVVTVPS SSLGTQTYIC NVNHKPSNTK VDKKVEPKSC DKHTHTCPPCP APELLGGPSV 240
FLFPPKPKDPT LMISRTPEVT CVVVDVSHED PEVKFNWYVD GVEVHNAKTK PREEQYNSTY 300
RVVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK GQPREPQVYT LPPSRDELTK 360
NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTTPVLDS DGSFFLYSKL TVDKSRWQQG 420
NVFSCSVMHE ALHNHYTQKS LSLSPGKSGG GGSELCDDDP PEI PHATFKA MAYKEGTM LN 480
CECKRGRFRI KSGSLYMLCT GNSHSSWDN QCQCTSSATR NTTKQVTPQP EEQKERKTE 540
MQSPMQPVDQ ASLPGHCREP PPWENEATER IYHFVVGQMV YYQCVQGYRA LHRGPAESVC 600
KMTHGKTRWT QPQLICTSGG GSGGGGSGG GSGGGGSAPT SSSTKKTQLQ LEHLLLDLQM 660
ILNGINNYKN PKLTRMLTFK FYMPKKATEL KHLQCLEEEL KPLEEVLNLA QSKNFHLRPR 720
DLISRINIV LELKGSSETF MCEYADETAT IVEFLNRWIT FCQSIISTLT 770

SEQ ID NO: 600                       moltype = AA length = 770
FEATURE                               Location/Qualifiers
source                                1..770
                                        mol_type = protein
                                        organism = Synthetic construct

SEQUENCE: 600
EVQLVESGGG LVQPGRSLKL SCAVSGFTFS DYAMAWVRQA PPKGLEWVAT ISYDGSRTYY 60
RDSVKGRFTI SRDNAKITLY LQMDSLRSER TATYYCARHG SGYPDYWGQG VMVTVSSAST 120
KGPSVFPPLAP SSKSTSGGTA ALGCLVKDYF PEPVTVSWNS GALTSGVHTF PAVLQSSGLY 180
SLSSVVTVPS SSLGTQTYIC NVNHKPSNTK VDKKVEPKSC DKHTHTCPPCP APELLGGPSV 240
FLFPPKPKDPT LMISRTPEVT CVVVDVSHED PEVKFNWYVD GVEVHNAKTK PREEQYNSTY 300
RVVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK GQPREPQVYT LPPSRDELTK 360
NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTTPVLDS DGSFFLYSKL TVDKSRWQQG 420
NVFSCSVMHE ALHNHYTQKS LSLSPGKSGG GGSELCDDDP PEI PHATFKA MAYKEGTM LN 480
CECKRGRFRI KSGSLYMLCT GNSHSSWDN QCQCTSSATR NTTKQVTPQP EEQKERKTE 540
MQSPMQPVDQ ASLPGHCREP PPWENEATER IYHFVVGQMV YYQCVQGYRA LHRGPAESVC 600
KMTHGKTRWT QPQLICTSGG GSGGGGSGG GSGGGGSAPT SSSTKKTQLQ LEHLLLDLQM 660
ILNGINNYKN PKLTRMLTFK FYMPKKATEL KHLQCLEEEL KPLEEVLNLA QSKNFHLRPR 720
DLISEINIV LELKGSSETF MCEYADETAT IVEFLNRWIT FCQSIISTLT 770

SEQ ID NO: 601                       moltype = AA length = 770
FEATURE                               Location/Qualifiers
source                                1..770
                                        mol_type = protein
                                        organism = Synthetic construct

SEQUENCE: 601
EVQLVESGGG LVQPGRSLKL SCAVSGFTFS DYAMAWVRQA PPKGLEWVAT ISYDGSRTYY 60
RDSVKGRFTI SRDNAKITLY LQMDSLRSER TATYYCARHG SGYPDYWGQG VMVTVSSAST 120
KGPSVFPPLAP SSKSTSGGTA ALGCLVKDYF PEPVTVSWNS GALTSGVHTF PAVLQSSGLY 180
SLSSVVTVPS SSLGTQTYIC NVNHKPSNTK VDKKVEPKSC DKHTHTCPPCP APELLGGPSV 240
FLFPPKPKDPT LMISRTPEVT CVVVDVSHED PEVKFNWYVD GVEVHNAKTK PREEQYNSTY 300
RVVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK GQPREPQVYT LPPSRDELTK 360
NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTTPVLDS DGSFFLYSKL TVDKSRWQQG 420
NVFSCSVMHE ALHNHYTQKS LSLSPGKSGG GGSELCDDDP PEI PHATFKA MAYKEGTM LN 480
CECKRGRFRI KSGSLYMLCT GNSHSSWDN QCQCTSSATR NTTKQVTPQP EEQKERKTE 540
MQSPMQPVDQ ASLPGHCREP PPWENEATER IYHFVVGQMV YYQCVQGYRA LHRGPAESVC 600
KMTHGKTRWT QPQLICTSGG GSGGGGSGG GSGGGGSAPT SSSTKKTQLQ LEHLLLDLQM 660
ILNGINNYKN PKLTRMLTFK FYMPKKATEL KHLQCLEEEL KPLEEVLNLA QSKNFHLRPR 720
DLISFINIV LELKGSSETF MCEYADETAT IVEFLNRWIT FCQSIISTLT 770

SEQ ID NO: 602                       moltype = AA length = 770
FEATURE                               Location/Qualifiers
source                                1..770
                                        mol_type = protein
                                        organism = Synthetic construct

SEQUENCE: 602
EVQLVESGGG LVQPGRSLKL SCAVSGFTFS DYAMAWVRQA PPKGLEWVAT ISYDGSRTYY 60
RDSVKGRFTI SRDNAKITLY LQMDSLRSER TATYYCARHG SGYPDYWGQG VMVTVSSAST 120
KGPSVFPPLAP SSKSTSGGTA ALGCLVKDYF PEPVTVSWNS GALTSGVHTF PAVLQSSGLY 180
SLSSVVTVPS SSLGTQTYIC NVNHKPSNTK VDKKVEPKSC DKHTHTCPPCP APELLGGPSV 240
FLFPPKPKDPT LMISRTPEVT CVVVDVSHED PEVKFNWYVD GVEVHNAKTK PREEQYNSTY 300
RVVSVLTVLH QDWLNGKEYK CKVSNKALPA PIEKTISKAK GQPREPQVYT LPPSRDELTK 360
NQVSLTCLVK GFYPSDIAVE WESNGQPENN YKTTTPVLDS DGSFFLYSKL TVDKSRWQQG 420
NVFSCSVMHE ALHNHYTQKS LSLSPGKSGG GGSELCDDDP PEI PHATFKA MAYKEGTM LN 480
CECKRGRFRI KSGSLYMLCT GNSHSSWDN QCQCTSSATR NTTKQVTPQP EEQKERKTE 540
MQSPMQPVDQ ASLPGHCREP PPWENEATER IYHFVVGQMV YYQCVQGYRA LHRGPAESVC 600
KMTHGKTRWT QPQLICTSGG GSGGGGSGG GSGGGGSAPT SSSTKKTQLQ LEHLLLDLQM 660
ILNGINNYKN PKLTRMLTFK FYMPKKATEL KHLQCLEEEL KPLEEVLNLA QSKNFHLRPR 720
DLISIINIV LELKGSSETF MCEYADETAT IVEFLNRWIT FCQSIISTLT 770

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SEQ ID NO: 603 moltype = AA length = 770
 FEATURE Location/Qualifiers
 source 1..770
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 603

| | | | | | | |
|-------------|-------------|------------|------------|------------|-------------|-----|
| EVQLVESGGG | LVQPGRSLKL | SCAVSGFTFS | DYAMAWVRQA | PKKGLEWVAT | ISYDGSRTYY | 60 |
| RDSVKGRFTI | SRDNAKITLY | LQMDSLRSED | TATYYCARHG | SGYFDYWQGG | VMVTVSSAST | 120 |
| KGPSVFPLAP | SSKSTSGGTA | ALGCLVKDYF | PEPVTVSWNS | GALTSGVHTF | PAVLQSSGLY | 180 |
| SLSSVVTVPS | SSLGTQTYIC | NVNHKPSNTK | VDKKVEPKSC | DKTHTCPPCP | APELLGGPSV | 240 |
| FLFPPKPKDT | LMI SRTPEVT | CVVVDVSHED | PEVKFNWYVD | GVEVHNAKTK | PREEQYNSTY | 300 |
| RVVSVLTVLH | QDWLNGKEYK | CKVSNKALPA | PIEKTISKAK | GQPREPQVYT | LPPSRDELTK | 360 |
| NQVSLTCLVK | GFYPSDIAVE | WESNGQPENN | YKTPPVLDL | DGSFFLYSKL | TVDKSRWQQG | 420 |
| NVFCSCVMHE | ALHNHYTQKS | LSLSPGKSGG | GGSELCDDDP | PEIPHATFKA | MAYKEGTM LN | 480 |
| CECKRGRFRI | KSGSLYMLCT | GNSSHSSWDN | QCQCTSSATR | NTTKQVTPQP | EEQKERKTE | 540 |
| MQSPMQPVDQ | ASLPGHCREP | PPWENEATER | IYHFVVGQMV | YYQCVQGYRA | LHRGPAESVC | 600 |
| KMTHGKTRWT | QPQLICTSGG | GGSGGGSGG | GGSGGGSAPT | SSSTKKTQLQ | LEHLLLDLQM | 660 |
| ILNGINNYKN | PKLTRMLTFK | FYMPKKATEL | KHLQCLEEEL | KPLEEVLNLA | QSKNFHLRPR | 720 |
| DLISNINIVAV | LELKGSETTF | MCEYADETAT | IVEFLNRWIT | FCQSIISTLT | | 770 |

SEQ ID NO: 604 moltype = AA length = 770
 FEATURE Location/Qualifiers
 source 1..770
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 604

| | | | | | | |
|-------------|-------------|------------|------------|------------|-------------|-----|
| EVQLVESGGG | LVQPGRSLKL | SCAVSGFTFS | DYAMAWVRQA | PKKGLEWVAT | ISYDGSRTYY | 60 |
| RDSVKGRFTI | SRDNAKITLY | LQMDSLRSED | TATYYCARHG | SGYFDYWQGG | VMVTVSSAST | 120 |
| KGPSVFPLAP | SSKSTSGGTA | ALGCLVKDYF | PEPVTVSWNS | GALTSGVHTF | PAVLQSSGLY | 180 |
| SLSSVVTVPS | SSLGTQTYIC | NVNHKPSNTK | VDKKVEPKSC | DKTHTCPPCP | APELLGGPSV | 240 |
| FLFPPKPKDT | LMI SRTPEVT | CVVVDVSHED | PEVKFNWYVD | GVEVHNAKTK | PREEQYNSTY | 300 |
| RVVSVLTVLH | QDWLNGKEYK | CKVSNKALPA | PIEKTISKAK | GQPREPQVYT | LPPSRDELTK | 360 |
| NQVSLTCLVK | GFYPSDIAVE | WESNGQPENN | YKTPPVLDL | DGSFFLYSKL | TVDKSRWQQG | 420 |
| NVFCSCVMHE | ALHNHYTQKS | LSLSPGKSGG | GGSELCDDDP | PEIPHATFKA | MAYKEGTM LN | 480 |
| CECKRGRFRI | KSGSLYMLCT | GNSSHSSWDN | QCQCTSSATR | NTTKQVTPQP | EEQKERKTE | 540 |
| MQSPMQPVDQ | ASLPGHCREP | PPWENEATER | IYHFVVGQMV | YYQCVQGYRA | LHRGPAESVC | 600 |
| KMTHGKTRWT | QPQLICTSGG | GGSGGGSGG | GGSGGGSAPT | SSSTKKTQLQ | LEHLLLDLQM | 660 |
| ILNGINNYKN | PKLTRMLTFK | FYMPKKATEL | KHLQCLEEEL | KPLEEVLNLA | QSKNFHLRPR | 720 |
| DLISNINIVIV | LALKGSETTF | MCEYADETAT | IVEFLNRWIT | FCQSIISTLT | | 770 |

SEQ ID NO: 605 moltype = AA length = 770
 FEATURE Location/Qualifiers
 source 1..770
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 605

| | | | | | | |
|-------------|-------------|------------|------------|------------|-------------|-----|
| EVQLVESGGG | LVQPGRSLKL | SCAVSGFTFS | DYAMAWVRQA | PKKGLEWVAT | ISYDGSRTYY | 60 |
| RDSVKGRFTI | SRDNAKITLY | LQMDSLRSED | TATYYCARHG | SGYFDYWQGG | VMVTVSSAST | 120 |
| KGPSVFPLAP | SSKSTSGGTA | ALGCLVKDYF | PEPVTVSWNS | GALTSGVHTF | PAVLQSSGLY | 180 |
| SLSSVVTVPS | SSLGTQTYIC | NVNHKPSNTK | VDKKVEPKSC | DKTHTCPPCP | APELLGGPSV | 240 |
| FLFPPKPKDT | LMI SRTPEVT | CVVVDVSHED | PEVKFNWYVD | GVEVHNAKTK | PREEQYNSTY | 300 |
| RVVSVLTVLH | QDWLNGKEYK | CKVSNKALPA | PIEKTISKAK | GQPREPQVYT | LPPSRDELTK | 360 |
| NQVSLTCLVK | GFYPSDIAVE | WESNGQPENN | YKTPPVLDL | DGSFFLYSKL | TVDKSRWQQG | 420 |
| NVFCSCVMHE | ALHNHYTQKS | LSLSPGKSGG | GGSELCDDDP | PEIPHATFKA | MAYKEGTM LN | 480 |
| CECKRGRFRI | KSGSLYMLCT | GNSSHSSWDN | QCQCTSSATR | NTTKQVTPQP | EEQKERKTE | 540 |
| MQSPMQPVDQ | ASLPGHCREP | PPWENEATER | IYHFVVGQMV | YYQCVQGYRA | LHRGPAESVC | 600 |
| KMTHGKTRWT | QPQLICTSGG | GGSGGGSGG | GGSGGGSAPT | SSSTKKTQLQ | LEHLLLDLQM | 660 |
| ILNGINNYKN | PKLTRMLTFK | FYMPKKATEL | KHLQCLEEEL | KPLEEVLNLA | QSKNFHLRPR | 720 |
| DLISNINIVIV | LKLGSETTF | MCEYADETAT | IVEFLNRWIT | FCQSIISTLT | | 770 |

SEQ ID NO: 606 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 606

| | | | | | | |
|------------|------------|------------|------------|------------|------------|-----|
| APTSSSTKKT | QLQLEHLLLR | LQMILNGINN | YKNPKLTEML | TFKPYMPKKA | TELKHLQCLE | 60 |
| EELKPLEEVL | NLAQSKNFHL | RPRDLISNIN | VIVLELKGSE | TFMCEYADE | TATIVEFLNR | 120 |
| WITFCQSIIS | TLT | | | | | 133 |

SEQ ID NO: 607 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 607

| | | | | | | |
|------------|------------|------------|------------|------------|------------|-----|
| APTSSSTKKT | QLQLEHLLLN | LQMILNGINN | YKNPKLTEML | TFKPYMPKKA | TELKHLQCLE | 60 |
| EELKPLEEVL | NLAQSKNFHL | RPRDLISNIN | VIVLELKGSE | TFMCEYADE | TATIVEFLNR | 120 |
| WITFCQSIIS | TLT | | | | | 133 |

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SEQ ID NO: 608 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 608
APTSSSTKKT QLQLEHLLQ LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 609 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 609
APTSSSTKKT QLQLEHLLLE LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 610 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 610
APTSSSTKKT QLQLEHLLLG LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 611 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 611
APTSSSTKKT QLQLEHLLLI LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 612 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 612
APTSSSTKKT QLQLEHLLL LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 613 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 613
APTSSSTKKT QLQLEHLLLK LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 614 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 614
APTSSSTKKT QLQLEHLLLM LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
WITFCQSIIS TLT 133

SEQ ID NO: 615 moltype = AA length = 133
FEATURE Location/Qualifiers
source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 615
APTSSSTKKT QLQLEHLLLF LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120

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WITFCQSIIS TLT 133

SEQ ID NO: 616 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 616
 APTSSSTKKT QLQLEHLLLP LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
 EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 617 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 617
 APTSSSTKKT QLQLEHLLLT LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
 EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 618 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 618
 APTSSSTKKT QLQLEHLLLV LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
 EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 619 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 619
 APTSSSTKKT QLQLEHLLLY LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
 EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 620 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = Synthetic construct

SEQUENCE: 620
 APTSSSTKKT QLQLEHLLLV LQMILNGINN YKNPKLTEML TFKFYMPKKA TELKHLQCLE 60
 EELKPLEEVL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

SEQ ID NO: 621 moltype = AA length = 133
 FEATURE Location/Qualifiers
 source 1..133
 mol_type = protein
 organism = synthetic construct

SEQUENCE: 621
 APTSSSTKKT QLQLEHLLLD LQMILNGINN YKNPKLTRML TKKFRMPKKA TELKHLQCLE 60
 EELKPLEERL NLAQSKNFHL RPRDLISNIN VIVLELKGSE TTFMCEYADE TATIVEFLNR 120
 WITFCQSIIS TLT 133

What is claimed:

1. An anti-human PD-1 (hPD-1) antibody-modified human interleukin-2 (hIL-2) immunoconjugate comprising: a modified hIL-2 protein comprising the amino acid sequence of SEQ ID NO: 217; and an anti-hPD-1 antibody, or antigen-binding fragment thereof, that immunospecifically binds to hPD-1, wherein the antibody or antigen-binding fragment thereof, comprises a heavy chain complementarity determining region 1 (CDR1) comprising the amino acid sequence of SEQ ID NO: 418, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 419, a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 420, a light chain CDR1

comprising the amino acid sequence of SEQ ID NO: 421, a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 422, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 423.

2. The immunoconjugate of claim 1, wherein the anti-hPD-1 antibody, or antigen-binding fragment thereof, comprises an IgG1 heavy chain constant region.

3. The immunoconjugate of claim 2, wherein the anti-hPD-1 antibody, or antigen-binding fragment thereof, comprises an L235A substitution and a G237A substitution, according to EU numbering.

4. The immunoconjugate of claim 3, wherein the anti-hPD-1 antibody, or antigen-binding fragment thereof, com-

415

prises a heavy chain (HC) comprising the amino acid sequence of SEQ ID NO: 414 and a light chain (LC) comprising the amino acid sequence of SEQ ID NO: 415.

5 **5.** An anti-hPD-1 antibody-modified hIL-2 immunoconjugate comprising:

a modified hIL-2 protein comprising the amino acid sequence of SEQ ID NO: 217; and

an anti-hPD-1 antibody, or antigen-binding fragment thereof, comprising a VH comprising the amino acid sequence of SEQ ID NO: 416 and a VL comprising the amino acid sequence of SEQ ID NO: 417.

6. The immunoconjugate of claim **5**, wherein the anti-hPD-1 antibody, or antigen-binding fragment thereof, comprises an IgG1 heavy chain constant region.

7. The immunoconjugate of claim **6**, wherein the anti-hPD-1 antibody, or antigen-binding fragment thereof, comprises an L235A substitution and a G237A substitution, according to EU numbering.

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8. The immunoconjugate of claim **7**, wherein the anti-hPD-1 antibody, or antigen-binding fragment thereof, comprises a HC comprising the amino acid sequence of SEQ ID NO: 414 and a LC comprising the amino acid sequence of SEQ ID NO: 415.

9. An anti-hPD-1 antibody-modified hIL-2 immunoconjugate comprising:

a modified hIL-2 protein comprising the amino acid sequence of SEQ ID NO: 217; and

10 an anti-hPD-1 antibody, or antigen-binding fragment thereof, comprising a HC comprising the amino acid sequence of SEQ ID NO: 414 and a LC comprising the amino acid sequence of SEQ ID NO: 415.

10. The immunoconjugate of claim **9**, comprising:
15 a light chain comprising the amino acid sequence of SEQ ID NO: 415; and

a heavy chain-modified hIL-2 protein fusion comprising the amino acid sequence of SEQ ID NO: 532.

* * * * *